UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2019

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number 001-38503

Iterum Therapeutics plc
(Exact name of Registrant as specified in its Charter)

Ireland	**98-1283148**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

Block 2 Floor 3, Harcourt Centre,
Harcourt Street,
Dublin 2, Ireland
(Address of principal executive offices)

Not applicable
(Zip Code)

(+353) 1 903-8920
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Shares, $0.01 par value per share	ITRM	The Nasdaq Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Act). YES ☐ NO ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the Registrant's ordinary shares, $0.01 par value per share, on the Nasdaq Global Market on June 28, 2019, the last business day of the Registrant's most recently complete second fiscal quarter was $36,871,186.

The number of shares of Registrant's ordinary shares outstanding as of February 29, 2020 was 14,868,973.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "seek," "should," "target," "will," "would," or the negative of these words or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our use of cash reserves;
- the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the potential advantages of our product candidates;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization of our product candidates, if approved;
- our ability to draw down our second term loan with Silicon Valley Bank;
- our manufacturing plans;
- our sales, marketing and distribution capabilities and strategy;
- market acceptance of any product we successfully commercialize;
- the pricing, coverage and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- our ability to enter into strategic arrangements, collaborations and/or commercial partnerships in the United States and other territories and the potential benefits of such arrangements;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- our expectations regarding how far into the future our cash on hand will fund our ongoing operations;
- our financial performance; and
- developments relating to our competitors and our industry.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in "Risk Factors" and elsewhere in this Annual Report. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Annual Report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Annual Report to conform these statements to new information, actual results or to changes in our expectations, except as required by law.

You should read this Annual Report and the documents that we have filed with the Securities and Exchange Commission, or SEC, as exhibits to this Annual Report with the understanding that our actual future results, levels of activity, performance, and events and circumstances may be materially different from what we expect.

This Annual Report also contains industry, market and competitive position data from our own internal estimates and research as well as industry and general publications and research surveys and studies conducted by third parties. Industry publications, studies, and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our internal data and estimates are based upon information obtained from trade and business organizations and other contacts in the markets in which we operate and our management's understanding of industry conditions. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal company research is reliable and the market definitions are appropriate, neither such research nor these definitions have been verified by any independent source. The industry in which we operate is subject to a high degree of uncertainty and risks due to various factors, including those described in the section titled "Risk Factors."

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

PART I

Item 1. Business.

Overview

We are a pharmaceutical company dedicated to developing and commercializing sulopenem to be potentially the first and only oral and intravenous (IV) branded penem available globally. Penems, including thiopenems and carbapenems, belong to a class of antibiotics more broadly defined as ß-lactam antibiotics, the original example of which was penicillin, but which now also includes cephalosporins. Sulopenem is a potent, thiopenem antibiotic delivered intravenously which is active against bacteria that belong to the group of organisms known as gram-negatives and cause urinary tract and intra-abdominal infections. We have also successfully developed sulopenem in an oral tablet formulation, sulopenem etzadroxil-probenecid. Both sulopenem product candidates have the potential to be important new treatment alternatives to address growing concerns related to antibacterial resistance without the known toxicities of some of the most widely used antibiotics, specifically fluoroquinolones. We see two distinct opportunities for our sulopenem program: patients at elevated risk for treatment failure in the community setting suffering from uncomplicated urinary tract infections (uUTI) and hospitalized patients suffering from complicated, antibiotic-resistant infections. During the third quarter of 2018, we initiated all three clinical trials in our Phase 3 development program, which includes: a Phase 3 uUTI, clinical trial, known as Sulopenem for Resistant Enterobacteriaceae (SURE) 1, comparing oral sulopenem to oral ciprofloxacin in women with uUTI, a Phase 3 complicated urinary tract infection (cUTI), clinical trial known as SURE 2, comparing IV sulopenem followed by oral sulopenem to IV ertapenem followed by oral ciprofloxacin in adults with cUTI, and a Phase 3 complicated intra-abdominal infection (cIAI) clinical trial known as SURE 3, comparing IV sulopenem followed by oral sulopenem to IV ertapenem followed by a combination of oral ciprofloxacin and oral metronidazole in adults with cIAI. We designed one Phase 3 clinical trial in each indication based on our end of Phase 2 meeting with the U.S. Food and Drug Administration (FDA) and feedback from the European Medicines Agency (EMA). We are conducting these three Phase 3 clinical trials under Special Protocol Assessment (SPA) agreements from the FDA. We completed enrollment in our uUTI and cUTI clinical trials in the fourth quarter of 2019 and expect to produce topline data around the end of the first quarter of 2020. If these data are positive, we expect to have an opportunity to file two new drug applications (NDAs), one for oral sulopenem and one for IV sulopenem, around mid-2020, which we expect would enable potential FDA approval in the first half of 2021. In December 2019, we announced that sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy for the cIAI trial; however, we believe the secondary supporting analyses and safety data support the potential of sulopenem in the treatment of multi-drug resistant infections. EMA Scientific Advice received by us, consistent with the existing Guidance for this indication, supports an endpoint assessed earlier than the primary study endpoint and a non-inferiority margin of -12.5%.

In November 2015, we acquired an exclusive, worldwide license under certain patents and know-how to develop and commercialize sulopenem and its oral prodrug, sulopenem etzadroxil, from Pfizer Inc. (Pfizer). Pfizer conducted Phase 1 and Phase 2 clinical trials of sulopenem delivered intravenously in Japan in over 1,450 patients with a variety of hospital and community acquired infections. These clinical trials documented a treatment effect in the indications studied and provided preliminary insights into the safety profile for sulopenem, which will continue to be assessed with additional clinical trials. Pfizer subsequently developed sulopenem into a prodrug formulation, sulopenem etzadroxil, to enable oral delivery. Once this prodrug is absorbed in the gastrointestinal tract, the etzadroxil ester is immediately cleaved off and the active moiety, sulopenem, is released into the bloodstream. We have further enhanced this prodrug formulation with the addition of probenecid to extend sulopenem's half-life and enhance its antibacterial potential. Probenecid is a pharmacokinetic enhancer that has been safely and extensively used globally for decades. The oral dose of sulopenem etzadroxil-probenecid has been combined in a single bilayer tablet, which we refer to as oral sulopenem. We refer to sulopenem delivered intravenously as sulopenem and, together with oral sulopenem, as our sulopenem program.

The treatment of urinary tract and intra-abdominal infections has become more challenging because of the development of resistance by pathogens responsible for these diseases. There are approximately 13.5 million emergency room and office visits for symptoms of urinary tract infections (UTIs) and approximately 21 million uUTIs in the United States annually. Based on market research, physicians estimated that approximately 35% of these patients are at elevated risk for treatment failure. Proper antibiotic treatment of drug-resistant infections in this group is particularly important due to the risks associated with treatment failure. Elevated risk patients were defined in the research as patients with recurrent UTIs, elderly patients, patients who have a suspected or confirmed drug-resistant infection, patients with comorbidities (e.g., Diabetes mellitus) or that are immunocompromised, patients that have had a recent hospitalization, patients with a history of prior antibiotic failure and patients in a long-term care setting. Treatment failures pose significant clinical and economic challenges to the healthcare system. There are also approximately 3.6 million patients with cUTI and approximately 350,000 patients with cIAI that require antibiotic therapy every year in the United States.

Growing antibiotic resistance to *E. coli,* the primary cause of UTIs, has complicated the choice of treatment alternatives in both the community and hospital settings, reducing effective treatment choices for physicians. In addition, the Infectious Diseases Society

of America and European Society for Microbiology and Infectious Diseases recommend against empiric use, or prescribing without results from a bacterial culture, of fluoroquinolones for uUTIs in their 2010 Update to the International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women. Similarly, the FDA in its November 2015 Advisory Committee meeting stated that the risk of serious side effects caused by fluoroquinolones generally outweighs the benefits for patients with uUTIs and other uncomplicated infections. Subsequently, the FDA mandated labeling modifications for fluoroquinolone antibiotics directing healthcare professionals to reserve fluoroquinolones for patients with no other treatment alternatives. In December 2018, the FDA further warned that fluoroquinolone antibiotics could cause aortic aneurysm and dissection in certain patients, especially older persons. In October 2018, the EMA's pharmacovigilance risk assessment committee recommended restrictions on the use of broad-spectrum antibiotics, fluoroquinolones and quinolones, following a review of side effects that were reported to be "disabling and potentially long-lasting." The committee further stated that fluoroquinolones and quinolones should only be used to treat infections where an antibiotic is essential, and others cannot be used.

None of the most commonly used oral antibiotics for treatment of uUTIs were initially approved by the FDA within the last two decades. We believe oral sulopenem will be an important empiric treatment option for elevated risk uUTI patients because of its potency against resistant pathogens, as well as its spectrum of antibacterial activity. In addition, oral sulopenem will allow patients who develop an infection with a resistant pathogen but are stable enough to be treated in the community, to avoid the need for an IV catheter and even hospitalization. The primary endpoint of our uUTI Phase 3 clinical trial is designed to demonstrate non-inferiority in patients with ciprofloxacin-susceptible pathogens but also provides an opportunity to demonstrate superiority to ciprofloxacin for oral sulopenem in patients with ciprofloxacin-resistant pathogens.

In the hospital setting, the lack of effective oral stepdown options results in the potential for lengthy hospital stays or insertion of a peripherally inserted central catheter (PICC) to facilitate administration of IV antibiotics, even for some patients with relatively straightforward infections. Our sulopenem program may enable faster discharges, providing cost-saving advantages for the hospital and mitigating the risk of catheter-related infection for patients. Based on potency, safety and formulation advantages, we believe our sulopenem program is uniquely positioned to address unmet medical needs for patients suffering from uncomplicated and complicated infections in both the community and hospital settings.

If the FDA approves oral sulopenem and sulopenem, we plan to seek a commercial partner and/or build a commercial infrastructure to launch both product candidates in the United States. Data from an ongoing epidemiology study to quantify quinolone resistance by zip code, in addition to data from our clinical trials and available prescriber data, will inform our initial targeted sales force as to where the medical need for a new, effective therapy for UTIs is highest in the community and hospital settings. Outside of the United States, we are evaluating our options to maximize the value of our sulopenem program.

We expect to register two suppliers and validate at least one supplier for the manufacture of the active pharmaceutical ingredient (API) at the time of our planned regulatory filings in the United States. We will initially rely on a single third-party facility to manufacture all of our sulopenem tablets. In the future, given the importance of oral sulopenem to our potential commercial results, we will consider establishing additional sources.

Our patent portfolio for sulopenem contains one exclusively licensed U.S. patent directed to composition of matter of sulopenem etzadroxil which is projected to expire in 2029, subject to potential extension to 2034 under the Drug Price Competition and Patent Term Restoration Act of 1984 or, the Hatch-Waxman Act and three exclusively licensed foreign patents. Our patent portfolio also contains two U.S. and international patent applications, one addressing the effect of probenecid on the plasma concentrations of sulopenem after multi-day dosing and the second related to a method of preparing a bilayer tablet composed of sulopenem etzadroxil and probenecid which resulted in an increase in the amount of sulopenem in the blood relative to dosing each agent in a separate formulation. Any U.S. or foreign patent issuing from the pending applications is projected to expire in 2039, excluding any additional term for patent adjustments or patent term extensions. In addition, the FDA has designated sulopenem and oral sulopenem as Qualified Infectious Disease Products (QIDP) for the indications of uUTI, cUTI, cIAI, community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease pursuant to the Generating Antibiotic Incentives Now Act (the GAIN Act). Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. QIDP status makes sulopenem and oral sulopenem eligible to benefit from certain incentives for the development of new antibiotics provided under the GAIN Act. Further, QIDP status could add five years to any regulatory exclusivity period that we may be granted. QIDP status for other indications is also possible given the coverage of gram-negative and gram-positive bacteria by sulopenem, pending submission of additional documentation and acceptance by the FDA. Fast track status provides an opportunity for more frequent meetings with the FDA, more frequent written communication related to the clinical trials, eligibility for accelerated approval and priority review and the potential for a rolling review. None of our licensed patents cover the IV formulation of sulopenem.

Sulopenem Program, Clinical and Regulatory Status

We pursued three initial indications for oral sulopenem and sulopenem in three Phase 3 clinical trials. We designed these Phase 3 clinical trials based on extensive *in vitro* microbiologic surveillance data, Phase 1 pharmacokinetic data from healthy volunteers as well as population pharmacokinetic data from patients, animal models in relevant disease settings, Phase 2 data from a program performed with sulopenem by Pfizer in Japan in the early 1990s, and regulatory feedback from the FDA at our end-of-Phase 2 meeting, all supported by an advanced commercial manufacturing program which provided clinical supplies.

In the third quarter of 2018 we initiated all three Phase 3 clinical trials, which are being conducted under SPA agreements from the FDA and completed enrollment in the fourth quarter of 2019. Topline data from our cIAI trial readout in the fourth quarter of 2019 and showed that the primary endpoint was narrowly missed. However, other key secondary efficacy analyses support the potential of sulopenem in the treatment of multi-drug resistant infections. Topline data from our cUTI and uUTI trials is expected around the end of the first quarter of 2020. If these data are positive, we expect to have an opportunity to file two NDAs, one for oral sulopenem and one for IV sulopenem, around mid-2020. Further, the QIDP designation of sulopenem and oral sulopenem provides for a six-month review period following the acceptance of our filings, starting typically at Day 60, which we expect would enable potential FDA approval in the first half of 2021. In preparation for a potential NDA filing, we recently gained alignment with FDA at a pre-NDA meeting regarding the filing package required for submission of our chemistry, manufacturing and controls (CMC) program.

Our Strategy

Our strategy is to develop and commercialize our sulopenem program for multiple indications, and in the long term to build a market-leading anti-infective business. The key elements of this strategy include the following:

- ***Complete sulopenem clinical development in three initial indications.*** Conduct single Phase 3 clinical trials in each of our three initial indications: uUTI, cUTI and cIAI. All three clinical trials were initiated in the third quarter of 2018 and completed enrollment by the end of 2019. Topline data from our cIAI trial readout in the fourth quarter of 2019 and showed that the primary endpoint was narrowly missed. However, other key secondary efficacy analyses support the potential of sulopenem in the treatment of multi-drug resistant infections. Topline data on our cUTI and uUTI trials is expected around the end of the first quarter of 2020. Each of these trials is being conducted under a SPA agreement with the FDA.
- ***Obtain regulatory approval for oral sulopenem and sulopenem in the United States and subsequently in the European Union.*** We designed our Phase 3 clinical program based on extensive discussions with the FDA, including our end-of-Phase 2 meeting in July 2017, and considered scientific advice received from the EMA to meet the regulatory filing requirements in the European Union. If our remaining Phase 3 clinical trials in cUTI and uUTI are successful, we plan to submit NDAs for both oral sulopenem and sulopenem to the FDA around mid-2020 and subsequently submit a Marketing Authorization Application (MAA) to the EMA in the second half of 2020.
- ***Maximize commercial potential of our sulopenem program.*** If approved, we intend to seek a commercial partner and/or directly commercialize our sulopenem program in the United States with a targeted sales force across the community and hospital settings. Outside of the United States, we are evaluating our options to maximize the value of our sulopenem program.
- ***Pursue the development of oral sulopenem and sulopenem in additional indications.*** In the future, we may pursue development of our sulopenem program in additional indications in adults and children, including community acquired bacterial pneumonia, bacterial prostatitis, diabetic foot infection and bone and joint infection, as well as new formulations to support these indications.
- ***Build a portfolio of differentiated anti-infective products.*** We intend to enhance our product pipeline through strategically in-licensing or acquiring clinical stage product candidates or approved products for the community and/or hospital and acute care markets. We believe that our focus on acute care in both the community and hospital markets will make us an attractive partner for companies seeking to out-license products or product candidates in our areas of focus.

The Medical Need

Urinary Tract and Intra-Abdominal Infections

UTIs are among the most common bacterial infections encountered in the ambulatory setting. A UTI occurs when one or more parts of the urinary system (kidneys, ureters, bladder or urethra) become infected with a pathogen (most frequently, bacteria). While many UTIs are not considered life-threatening, if the infection reaches the kidneys, serious illness, and even death, can occur. UTI diagnoses are stratified between either complicated or uncomplicated infections. uUTI refers to the invasion of a structurally and functionally normal urinary tract by a nonresident infectious organism (e.g., acute cystitis), and is diagnosed and commonly treated in an outpatient setting with an oral agent. Conversely, cUTIs, including acute pyelonephritis, are defined as a UTI ascending from the bladder accompanied by local and systemic signs and symptoms, including fever, chills, malaise, flank pain, back pain, and/or costo-

vertebral angle pain or tenderness, that occur in the presence of a functional or anatomical abnormality of the urinary tract or in the presence of catheterization, with treatment typically initiated by IV therapy in a hospital setting.

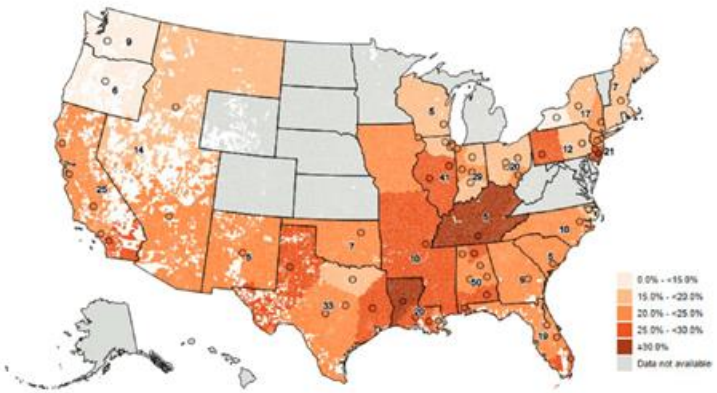
cIAIs have similar challenges to those of cUTIs. These complicated infections extend from a gastrointestinal source, such as the appendix or the colon, into the peritoneal space and can be associated with abscess formation.

Antimicrobial Resistance is Increasing

E. coli is growing increasingly resistant to many classes of antibiotics, which is especially problematic for patients suffering from UTIs because *E. coli* is the primary cause of those infections. The market-leading antibiotics, fluoroquinolones (e.g., Cipro, Levaquin) and trimethoprim-sulfamethoxazole (e.g., Bactrim, Septra), currently have *E. coli* resistance rates over 20% nationally. In 2015, approximately 75% of oral prescriptions for UTIs written in the United States were for fluoroquinolones or trimethoprim-sulfamethoxazole. In hospitals, fluoroquinolones have greater than 30% resistance to *E. coli* in approximately half the states in the United States, and have greater than 25% resistance rates in nearly 80% of the states. Between 2000 and 2009 the prevalence of extended spectrum ß-lactamases (ESBL)-producing *E. coli* and ESBL-producing *K. pneumoniae* more than doubled from 3.3% to 8.0% and from 9.1% to 18.6%, respectively. During the same timeframe, hospitalizations caused by ESBL-producing organisms increased by about 300%. The national resistance rate of *E. coli* to cephalosporins was estimated to be approximately 13% for the combined years of 2011 to 2015.

We have further delineated the prevalence of bacterial resistance to antibiotics used to treat UTIs in the United States. Based on urine culture results obtained at the zip code level from outpatient UTIs, we concluded that the prevalence of resistance of Enterobacteriaceae to quinolone antibiotics is over 20% in a significant portion of the country. In addition, in 2015, 25 states identified as high prevalence for *E. coli* resistance produced approximately 75% of all UTI prescriptions in the United States.

Geographic prevalence of quinolone non-susceptible Enterobacteriaceae by zip code in outpatient urine cultures.



Numbers represent hospital centers from which data were derived

As antibiotic resistance leads to increased costs of treatment and increased morbidity, as well as increased mortality, there is an urgent unmet medical need for antimicrobial agents that can be utilized in community and hospital infections. The antimicrobial class of penems has the potential to address many of the relevant resistance issues associated with ß-lactam antibiotics because of a targeted spectrum of antibacterial activity and intrinsic stability against hydrolytic attack by many ß-lactamases, including ESBL and AmpC enzymes.

There is a Significant Population at Risk

There are approximately 13.5 million emergency room and office visits for symptoms of UTIs and approximately 21 million uUTIs in the United States annually. Based on market research, physicians estimated that approximately 35% of these patients are at elevated risk for treatment failure. Proper antibiotic treatment of drug-resistant infections in this group is particularly important due to

the consequences associated with treatment failure. Elevated risk patients were defined in the research as patients with recurrent UTIs, elderly patients, patients who have a suspected or confirmed drug-resistant infection, patients with comorbidities (e.g., Diabetes mellitus) or that are immunocompromised, patients that have had a recent hospitalization, patients with a history of prior antibiotic failure and patients in a long-term care setting.

There are also approximately 3.6 million patients with cUTI and approximately 350,000 patients with cIAI that require antibiotic therapy every year in the United States.

Limited Treatment Options

In addition to worsening antibiotic resistance, many of the antibiotics currently used for first-line empiric oral treatment of uUTIs, such as nitrofurantoin and trimethoprim-sulfamethoxazole, suffer from significant safety and tolerability concerns. Pulmonary fibrosis and diffuse interstitial pneumonitis have been observed in patients treated with nitrofurantoin, which is contraindicated in pregnant women after 38 weeks of gestation and newborn children due to hemolytic anemia and in patients with poor renal function. Trimethoprim-sulfamethoxazole is associated with fatal hypersensitivity reactions, embryofetal toxicity, hyperkalemia, gastrointestinal disturbances and rashes, including rare cases of Stevens-Johnson Syndrome. In addition, some antibiotics, such as nitrofurantoin and fosfomycin, have poor tissue penetration. While fluoroquinolones are now the most widely used antibiotic class in treating community and hospital gram-negative infections, the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases now recommend against empiric use of fluoroquinolones for uUTIs in their 2010 Update to the International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women as they "have a propensity for collateral damage and should be reserved for important uses other than acute cystitis and thus should be considered alternative antimicrobials for acute cystitis." Similarly, the FDA in its November 2015 Advisory Committee meeting stated that the risk of serious side effects caused by fluoroquinolones generally outweighs the benefits for patients with uUTIs and other uncomplicated infections. Serious side effects associated with fluoroquinolones include tendon rupture, tendinitis, and worsening symptoms of myasthenia gravis and peripheral neuropathy. Subsequently, the FDA mandated labeling modifications for fluoroquinolones antibiotics directing healthcare professionals to reserve fluoroquinolones for patients with no other treatment alternatives. In December 2018 the FDA further warned that fluoroquinolone antibiotics could cause aortic aneurysm and dissection in certain patients, especially older persons. In October 2018, the EMA's pharmacovigilance risk assessment committee recommended restrictions on the use of broad-spectrum antibiotics, fluoroquinolones and quinolones, following a review of side effects that were reported to be "disabling and potentially long-lasting". The committee further stated that fluoroquinolones and quinolones should only be used to treat infections where an antibiotic is essential, and others cannot be used.

The limited oral antibiotic treatment options for patients with uUTIs can sometimes result in hospitalization to facilitate administration of IV antibiotics for patients whose infection progresses. In addition, some patients whose uUTI remains uncomplicated may require hospital admission for IV therapy. For patients with cUTIs, the lack of effective oral stepdown options, and the paucity of new treatment options, which is demonstrated by the fact that none of the most commonly used oral agents were initially approved by the FDA in the last two decades, results in the potential for lengthy hospital stays or insertion of a PICC to facilitate administration of IV antibiotics, even for some patients with relatively straightforward infections. Therefore, based both on the epidemiology described above and recent discussions with practicing clinicians and pharmacists, we believe there is a pressing need for a novel oral antibacterial therapy for UTI, both complicated and uncomplicated, that has potent activity against ESBL producing and quinolone resistant gram-negative organisms.

The Challenge of Developing Antibiotics

Antibiotics work by targeting a critical function of the bacteria and rendering it non-functional. These critical functions include the ability to make proteins, to replicate further, and to build protective envelopes against the harsh external environment. These functions are coded in the bacteria's DNA, which is copied over to each generation. Occasionally errors are made in the copying; typically, these errors kill off the progeny but can sometimes actually help them survive under specific circumstances, namely when threatened by an antibiotic.

Bacterial mutations, these changes in DNA coding, allow the organism to adapt their protein structures so as to prevent target-specific antibiotics from working. Over time, subsequent generations of bacteria retain these mutations and even develop additional mutations making them resistant to multiple classes of antibiotics and generating what is known as multi-drug resistant (MDR) pathogens. Furthermore, bacteria have also developed mechanisms that allow them to pass these genetic mutations directly to other nearby bacteria, even those from a different species. As there are a limited number of antibiotic classes available today, there is a concern that eventually we will not have any antibiotics to treat patients who develop an infection caused by these MDR bacteria. We continue to need new antibiotics that stay one step ahead of these mutating bacteria in order to protect against the infections that they cause.

The Solution to Rising Resistance

The solution to the problem of resistance is based on strategies to use those antibiotics only when patients really need them, limiting the number of opportunities for the bacteria to develop these mutations, and to continue efforts aimed at the discovery and development of new and effective antibacterial agents.

These new agents will need to:

- kill the organisms responsible for the actual infection;
- target a specific bacterial function and overcome the existing resistance mechanisms around that function;
- be powerful enough to require a minimal amount of drug to kill the organism at the site of infection; and
- be delivered to a patient in a manner which is safe, tolerable and convenient.

For the last thirty years, the penem class of antibiotics, including carbapenems such as imipenem, meropenem, doripenem and ertapenem, have been potent and reliable therapeutic options for patients with serious infections. Their spectrum of activity includes those pathogens responsible for infections such as those in the intra-abdominal space, urinary tract, and respiratory tract with a potency as good or better than any other antibiotic class, targeting the cell wall of bacteria, a critical element of bacterial defense. Resistance to the class, generally caused by organisms which have acquired a carbapenemase, is rarely, if ever, seen in the community setting and is primarily localized to patients with substantial healthcare exposures, particularly recent hospitalizations. These drugs are generally very well tolerated. Their limitation is the requirement to be delivered intravenously, restricting their utility to hospitalized patients.

Our Sulopenem Program

Our sulopenem program has the potential to offer a solution to the problem of antibiotic resistance and the limitations of existing agents. Sulopenem has *in vitro* activity against gram-negative organisms with resistance to one or more established antibiotics and can be delivered in an oral formulation. If a UTI occurs in the community setting, oral sulopenem can be provided as a tablet, offering an option for care of those with a culture proven or suspected MDR pathogen, potentially avoiding the need for hospitalization. If a patient requires hospitalization for an infection due to a resistant organism, treatment can be initiated intravenously with sulopenem and once the infection begins to improve, stepped down to oral sulopenem, potentially enabling the patient to leave the hospital.

Potential Advantages of Oral Sulopenem and Sulopenem

We are developing our sulopenem program to offer patients and clinical care providers a new option to treat drug-resistant gram-negative infections with confidence in its antimicrobial activity, and the flexibility to treat patients in the community while getting those hospitalized back home.

Sulopenem's differentiating characteristics include:

- ***Activity as an oral agent and favorable pharmacokinetic profile.*** Sulopenem is the active moiety with antibacterial activity. Oral sulopenem is a prodrug specifically selected among many other prodrug candidates because it enables the absorption of sulopenem from the gastrointestinal tract. It is this oral agent, sulopenem etzadroxil, combined with probenecid that we believe meets an urgent medical need to allow patients with resistant pathogens to be treated safely in the community, as well as allowing hospitalized patients to continue their treatment at home. Oral sulopenem is sufficiently absorbed from the gastrointestinal tract to allow the parent compound, sulopenem, to achieve adequate exposure in the tissues and, as demonstrated in animal models, to significantly reduce the burden of offending pathogens. Based on pharmacokinetic modeling and supported by prior clinical data from Japan, we believe dosing of the oral agent twice daily will provide tissue exposure sufficient to resolve clinical infection.
- ***Targeted spectrum of activity against relevant pathogens without pressure on other incidental gram-negative organisms.*** Sulopenem is active against the pathogens that are most likely to cause infection of the urinary and gastrointestinal tract, including *E. coli*, *K. pneumoniae*, *P. mirabilis* and *B. fragilis*. Like ertapenem, sulopenem is not active against certain gram-negative organisms such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. These organisms are not typically seen in community UTIs and are infrequently identified in UTIs in the hospital, except when patients have had an indwelling urinary catheter for an extended duration. As a result, we believe the targeted spectrum of sulopenem is less likely to put pressure on those pathogens which could otherwise have led to carbapenem resistance.
- ***Activity against multidrug resistant pathogens.*** Bacteria are accumulating resistance mechanisms to multiple classes of antibiotics within the same organism, and, as a consequence, physicians are losing confidence in existing antibiotics as

empiric therapy before culture results become available. Sulopenem is active against organisms that have multiple resistance mechanisms and can help avoid some of the consequences of ineffective antibiotic therapy.

- ***Documented safety and tolerability profile.*** Adverse event data collected as part of the Japanese Phase 2 development program conducted by Pfizer with the IV formulation provided preliminary insights into the safety profile for sulopenem, which will continue to be assessed with additional clinical trials. Data is also available for the oral formulation collected in healthy volunteers in the Phase 1 program conducted by us that is consistent with a well-tolerated regimen and similar to the adverse event profile observed with the IV formulation. One additional adverse event identified with the oral prodrug is loose stools, which were considered of mild severity and were self-limited, as seen with other broad spectrum oral antibiotics with activity against the anaerobic flora of the gastrointestinal tract. In the Japanese program, one patient reported a serious adverse event related to sulopenem of a transient elevation in liver function tests. The patient died due to metastatic lung cancer. Other serious adverse events recorded in patients receiving sulopenem in the Japanese program, which were not related by the investigator to sulopenem, included myocardial infarction with respiratory failure and progression of underlying ovarian carcinoma, in both cases resulting in death. For each of these patients, sulopenem was not determined to be the cause of death. In the recently completed cIAI Phase 3 clinical trial, among the 668 patients treated, treatment-related adverse events were observed in 6.0% and 5.1% of patients on sulopenem and ertapenem, respectively, with the most commonly reported drug-related adverse event being diarrhea, which was observed in 4.5% and 2.4% of patients on sulopenem and ertapenem, respectively. Discontinuations from treatment were uncommon for both regimens occurring in 1.5% of patients on sulopenem and 2.1% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 7.5% of patients on sulopenem and 3.6% of patients on ertapenem.
- ***Availability of an IV formulation.*** Sulopenem is expected to be available intravenously. Patients sick enough to require hospitalization may not be good candidates for initial oral therapy given potential uncertainties around the ability to absorb drugs due to diminished gastrointestinal and target tissue perfusion in patients with compromised cardiovascular status associated with sepsis or reduced gastrointestinal motility. An IV and oral formulation will enable the conduct of clinical registration trials in a manner consistent with typical clinical practice, allow for confidence in the initiation of therapy in seriously ill patients and, if approved, offer both important formulations as therapeutic options.
- ***Advanced manufacturing program.*** The synthetic pathway for sulopenem, initially defined in the 1980s, has now evolved through its third iteration, incorporating improvements in yield and scalability. We expect to register two different contract manufacturing organizations to manufacture the API for oral sulopenem and sulopenem. One manufacturer has completed process validation for oral sulopenem to date providing sufficient API for commercial launch if oral sulopenem is approved for marketing. We will initially rely on a single third-party facility to manufacture all of our sulopenem tablets. In the future, given the importance of sulopenem to our potential commercial results, we will consider establishing additional sources.

Market Opportunity for Oral Sulopenem and Sulopenem

Based upon the clinical evidence to date in eradicating key pathogens, coupled with unmet medical needs, if approved, we expect the commercial opportunity for oral sulopenem and sulopenem to be substantial with initial focus on the following areas:

- treating uUTI with an oral formulation in community treatment settings;
- treating cUTI with initiation of IV therapy in the hospital; and
- treating cUTI with an oral formulation upon discharge from hospital to complete therapy in the community setting.

Acute cystitis remains one of the most common indications for prescribing antimicrobials to otherwise healthy women, resulting in as many as 13.5 million office or emergency room visits in the United States annually, according to a review published in 2015. Up to 50% of all women experience one episode by 32 years of age. In addition, there are approximately 3.6 million patients a year in the United States for the more serious cases of cUTI.

In the United States, *E. coli* resistance presently exceeds 20% for fluoroquinolones, trimethoprim-sulfamethoxazole and ampicillin. Our market research indicated that physicians identified the lack of effective oral agents for these more difficult drug-resistant infections as a key unmet need in their practice. Physicians are particularly concerned by drug-resistant infections in the 35% of patients considered to be at elevated risk for treatment failure, as they pose significant potential clinical and economic challenges to the healthcare system when initial therapy is unsuccessful.

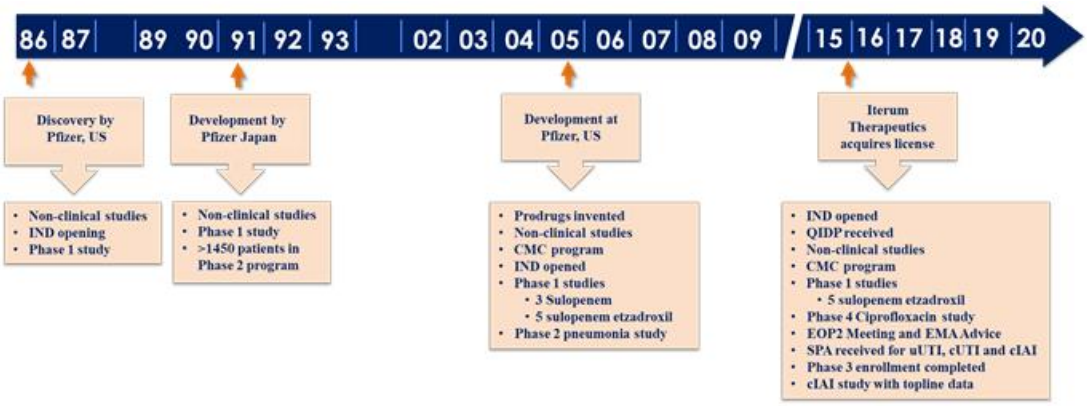
Given the growing prevalence of bacterial resistance that has rendered existing oral therapies ineffective, coupled with the FDA mandating new safety labeling changes to enhance warnings limiting fluoroquinolone use in uncomplicated infections due to the association with disabling and potentially permanent side effects, physicians are seeking new alternatives to safely and effectively treat their patients.

We believe oral sulopenem's value proposition will aid physicians in the community setting to address the unmet need for a safe and effective oral uUTI therapy to treat the growing number of patients with suspected or confirmed resistant pathogen(s). In addition, we believe our sulopenem program will offer a compelling value proposition to hospitals by enabling the transition of patients from IV therapy in the inpatient setting to an oral therapy in the community.

Oral Sulopenem and Sulopenem Clinical Development Program

The following graphic provides an overview of the past development of sulopenem etzadroxil and sulopenem by Pfizer and Iterum.

Discovery, Development, and Regulatory History of Sulopenem and Sulopenem Etzadroxil, by year



The objective of our sulopenem program is to deliver to patients an oral and IV formulation of sulopenem approved in the United States and Europe for the treatment of infections due to resistant gram-negative pathogens. Sulopenem's spectrum of activity, the availability of an oral agent delivered in a convenient dosing schedule and the evolving safety profile supported its further development for the target indications of uUTI, cUTI and cIAI. Oral sulopenem is the oral prodrug metabolized to sulopenem, its therapeutically active form, combined with probenecid.

Both sulopenem and oral sulopenem have received QIDP designation status for the indications of uUTI, cUTI and cIAI as well as for community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. QIDP designation status for other indications is also possible given the coverage of gram-negative and gram-positive bacteria by sulopenem, pending submission of additional documentation and acceptance by the FDA. We have received feedback on the development program in an end of Phase 2 meeting with the FDA, which provided guidance on the size of the safety database, the nonclinical study requirements, the design of the Phase 1 and Phase 3 clinical trials, the pediatric development plan, as well as support for the proposed CMC development activities through production of commercial supplies. The Phase 3 clinical trials for treatment of cIAI, cUTI and uUTI have received SPA agreements with the FDA. All three Phase 3 clinical trials were initiated in the third quarter of 2018 and completed enrollment by the end of 2019. Topline data for the cUTI and uUTI trials is expected around the end of the first quarter of 2020, and, if these data are positive, we expect to have the opportunity to file two NDAs, one for oral sulopenem and one for IV sulopenem, around mid-2020. In December 2019, we announced that sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy for the cIAI trial; however, we believe the secondary supporting analyses and safety data support the potential of sulopenem in the treatment of multi-drug resistant infections. EMA Scientific Advice received by us, consistent with the existing Guidance for this indication, supports an endpoint assessed earlier than the primary study endpoint and a non-inferiority margin of -12.5%. We also have an agreement with the FDA on a pediatric study plan. Development work on pediatric formulations is ongoing, and we plan to commence Phase 1 trials in children in 2020.

Microbiology Surveillance Data

Sulopenem has demonstrated potent *in vitro* activity, as defined by its minimum inhibitory concentration (MIC), against nearly all genera of Enterobacteriaceae, in anaerobes such as Bacteroides, Prevotella, Porphyromonas, Fusobacterium and Peptostreptococcus, gram-positive organisms including methicillin-susceptible staphylococci, *Streptococcus pyogenes* and *Streptococcus pneumoniae*, as well as other community respiratory pathogens such as *Haemophilus influenzae* and *Moraxella catarrhalis*. The MIC is a measure used to describe the results of an *in vitro* assay in which a fixed number of a strain of bacteria are

added to a 96-well plate and increasing concentrations of antibiotic are sequentially added to the wells. The concentration of antibiotic which inhibits growth of the bacteria in a well is considered the MIC. When looking across a collection of many strains of a species of bacteria, the MIC_{90} is the lowest concentration of antibiotic at which 90% of the strains are inhibited. Sulopenem lacks *in vitro* activity ($MIC_{90} \geq 16$ µg/mL) against the oxidative non-fermenting pathogens such as *Pseudomonas aeruginosa*, *Acinetobacter baumanii*, *Burkholderia cepacia*, and *Stenotrophomonas maltophilia.* Given its lack of potency against *Pseudomonas aeruginosa*, its use in treatment of infections caused by pathogenic Enterobacteriaceae should not select for pseudomonas resistant to carbapenems, as can occur with imipenem and meropenem. For various species of enterococci, the MIC_{90} values were 4 to ≥ 64 µg/mL. Methicillin-resistant staphylococci also have high MIC values.

The table below highlights the MIC_{50} and MIC_{90} of key target pathogens collected by International Health Management Associates (IHMA) between 2013 and 2015 responsible for the infections that will be studied in our Phase 3 program.

Organism Class	**N**	**MIC_{50} (µg/mL)**	**MIC_{90} (µg/mL)**
E. coli	189	0.015	0.03
ESBL negative	169	0.015	0.03
ESBL positive	20	0.03	0.06
Klebsiella spp.	124	0.03	0.06
ESBL negative	108	0.03	0.06
ESBL positive	16	0.03	0.25
P. mirabilis	14	0.12	0.25
E. aerogenes	57	0.06	0.25
C. koseri	60	0.03	0.03
S. marcescens	55	0.12	0.50
Gram-negative anaerobes	125	0.12	0.25
Staphylococcus saprophyticus	31	0.25	0.25

A comparison of the *in vitro* activity of sulopenem relative to other carbapenems, as well as to currently prescribed oral agents for UTI, is provided below. The activity of sulopenem at slightly higher doses was very similar to that of ertapenem and meropenem, which are currently commercially available. In addition, sulopenem is noted to have potent *in vitro* activity against relevant organisms that are resistant to fluoroquinolones and trimethoprim-sulfamethoxazole and are ESBL positive. The prevalence of resistance for the existing generic antibiotics, now exceeding 20% for many pathogens, underscores the challenge of treating patients with uUTI in an outpatient setting or releasing patients from the hospital with a cUTI or cIAI on a reliable stepdown oral therapy.

	***E. coli* N=189**		***K. pneumoniae* N=65**		***P. mirabilis* N=19**	
Penem Class:	**MIC_{90} (µg/mL)**	**% S**	**MIC_{90} (µg/mL)**	**% S**	**MIC_{90} (µg/mL)**	**% S**
Sulopenem	**0.06**	*	**0.12**	*	**0.25**	*
Ertapenem	0.015	100	0.12	97	0.03	100
Meropenem	0.03	100	0.06	97	0.12	100
Oral Agents Currently on Market:						
Nitrofurantoin	16	97	≥ 64	23	≥ 64	0
Fosfomycin	8	98	128	86	64	95
Ciprofloxacin	≥ 2	77	1	91	≥ 2	74
Trimethoprim-Sulfamethoxazole	≥ 32	74	≥ 32	86	≥ 32	58
Amoxicillin-Clavulanate	16	76	≥ 16	80	≥ 16	74

N = bacterial samples; each product candidate was tested using the same sample size

% S = percentage susceptible, meaning the proportion of the number of isolates tested that had a MIC below the FDA defined susceptibility breakpoint; boxed values signify a percentage susceptible below 80%, which is the threshold for concern for use of an antibiotic before a culture is available

* Susceptibility breakpoints are established by the FDA and documented in product labeling based on the antibacterial agent treatment efficacy in Phase 3 clinical trials associated with a specific MIC. As such, susceptibility breakpoints have not yet been determined for sulopenem.

Animal Models

Sulopenem reduced the bacterial burden in the bladder and tissues of infected animals in a uUTI model in both diabetic and normal C3H/HeN mice using a MDR ST131 *E. coli*, a strain which is ESBL positive and resistant to fluoroquinolones and trimethoprim-sulfamethoxazole. Sulopenem was highly efficacious and remarkably robust in its reduction in bacterial burden, leading to complete resolution of bacteriuria in all or most of the animals in both study arms with the high dose treatment regimen also reducing bacterial burden in bladder tissue and the kidney.

Non-clinical Pharmacology

Metabolic clearance is primarily characterized by hydrolysis of the ß-lactam ring. Sulopenem does not inhibit the major cytochrome P450 isoforms suggesting a low potential for drug interactions at therapeutic concentrations. It is predominantly excreted in the urine. Plasma protein binding for sulopenem is low at approximately 11%.

Phase 1 Program

The table below outlines the Phase 1 clinical trials that have been conducted with sulopenem etzadroxil and sulopenem.

Protocol	Year	Dose (mg), other medication	Subjects on sulopenem or sulopenem etzadroxil	Treatment (Days)
Sulopenem (CP-70,429)—Phase 1 Single Dose Clinical Trials				
A109001	1987	1000 mg	6	1
Japanese PK		250 mg, 500 mg, 1000 mg	18	1
A7371007	2007	400 mg, 800 mg, 1600 mg, 2400 mg, 2800 mg, placebo	24	1
IT001-105	2018	366 mg IV	34	1
Sulopenem (CP-70,429)—Phase 1 Multiple Dose Clinical Trials				
Japanese PK		500 mg, 1000 mg	12	5
Japanese PK		1000 mg	6	5
A1091001	2009	800 mg, 1200 mg, 1600 mg, 2000 mg, placebo	40	14
IT001-103	2019	1000 mg	15	2
IT001-104	2019	1000 mg	10	3
IT001-105	2018	1000 mg	12	3
Sulopenem etzadroxil (PF-03709270)—Phase 1 Single Dose Clinical Trials				
A8811001	2007	400 mg, 600 mg, 1000 mg, 2000 mg, placebo	9	1
A8811006	2008	2000 mg	4	1
A8811007	2007	600 mg, probenecid	4	1
A8811008	2008	1200 mg, probenecid	24	1
A8811018	2008	1000 mg, 1200 mg, probenecid, aluminum hydroxide, pantoprazole	17	1
A8811003	2008	2000 mg, 4000 mg, 6000 mg, 8000 mg, placebo	11	1
IT001-101	2017	500 mg, 1000 mg, probenecid	48	1
IT001-102	2017	500 mg, probenecid	13	1
Sulopenem etzadroxil (PF-03709270)—Phase 1 Multiple Dose Clinical Trials				
A8811003	2008	2000 mg, 1200 mg, probenecid, placebo	18	10
A8811015	2009	500 mg, 1000 mg, 1500 mg, probenecid, placebo, Augmentin	48	7
IT001-101	2017	500 mg, probenecid	64	7
IT001-103	2019	Bilayer tablet, 500 mg	47	2
IT001-104	2019	Bilayer tablet, 500 mg	19	3
IT001-105	2018	500 mg, bilayer tablet	34	2
Sulopenem (CP-70,429), Sulopenem etzadroxil (PF-03709270)—Phase 1 Renal Impairment Clinical Trial				
A8811009	2010	200mg, 800 mg sulopenem or 1000 mg sulopenem etzadroxil	29	1

Protocol	Year	Dose (mg), other medication	Subjects on sulopenem or sulopenem etzadroxil	Treatment (Days)
		Total	566	

Note: Total number reflects the sum of patients exposed to a specific formulation and dosing duration and will overestimate the number of subjects exposed as some subjects received more than one formulation in a study.

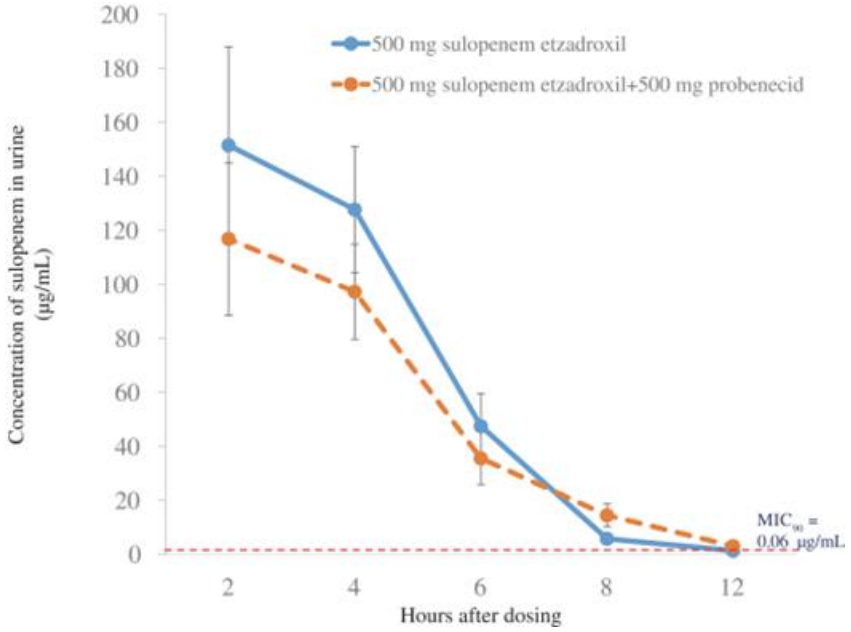
Oral Sulopenem

We have designed oral sulopenem to include probenecid, a pharmacokinetic enhancer that delays the excretion through the kidneys of sulopenem and other ß-lactam antibiotics and has been extensively used for this purpose and the treatment of gout. It enables us to maximize the antibacterial potential of any given dose of oral sulopenem.

We conducted three Phase 1 clinical trials, IT001-101, IT001-102 and IT001-105, in healthy volunteers, in part to select the prodrug and explore various doses of probenecid combined with 500 mg of sulopenem etzadroxil. Findings from these clinical trials are consistent with those from other pharmacokinetic studies that employed different total doses of sulopenem etzadroxil. Specifically, the AUC (area under the curve, a measure of total exposure) and Cmax (maximum plasma concentration) are generally dose-proportional, and the concomitant use of probenecid increases the plasma exposure of sulopenem with any dose with which it was studied.

The mean total sulopenem exposures in the urine after a single 500 mg dose in IT001-101 exceeded the MIC_{90} for the entire twice-daily dosing interval in the 32 healthy volunteers who received 500 mg of sulopenem etzadroxil, as illustrated in the graph below. In a urine antibacterial assay, urine collected at two hours post-dose was bactericidal for numerous strains of *E. coli* and *K. pneumoniae*, including a strain of *K. pneumoniae* that was resistant to meropenem and imipenem, with a sulopenem MIC of 16 µg/mL.

Mean total sulopenem exposure in urine after single 500 mg dose of sulopenem etzadroxil with or without probenecid



In IT001-102, we evaluated sulopenem etzadroxil administered with and without probenecid in a randomized cross-over trial in healthy volunteers in a fasted state. Subjects receiving sulopenem etzadroxil in a powder-in-a-bottle formulation co-administered with

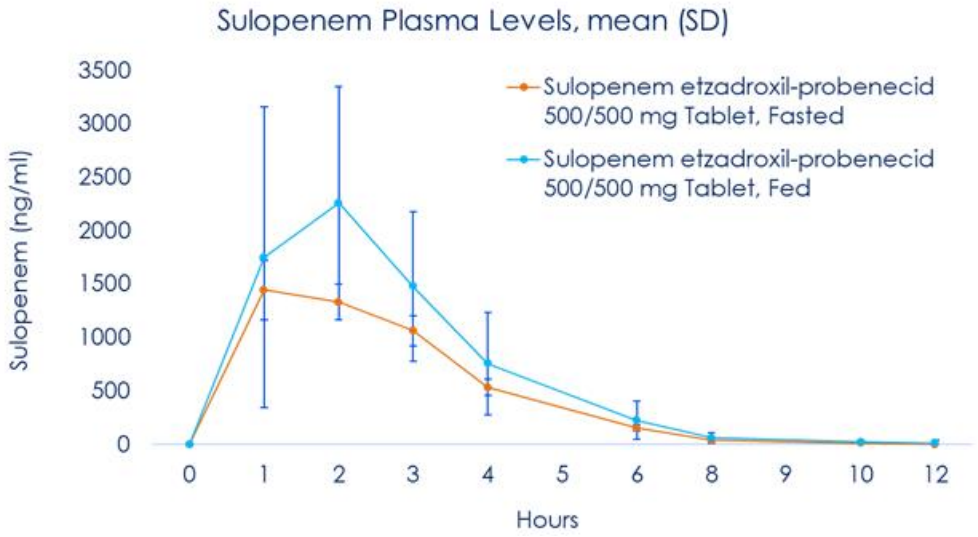
a separate tablet of probenecid demonstrated an increase in the time over MIC (of a 12 hour dosing interval) and AUC of sulopenem, as shown in the table below.

			Sulopenem Parameter (Day 1)			
Treatment	**N**	**Descriptive Statistic**	**Cmax (ng/mL)**	**AUC 0-¥ (hr*ng/mL)**	**T>MIC (0.5 µg/mL) [hr]**	**T>MIC (0.5 µg/mL) [%]**
500 mg Sulopenem etzadroxil	10	Mean	1928	3871	2.8	23.3
500 mg Sulopenem etzadroxil + 500 mg probenecid	11	Mean	1929	4964	3.6	30.2

N = number of subjects; Cmax = maximum plasma concentration; AUC0-¥ = area under the curve from the initiation of dosing extrapolated through infinite time

In addition, results from IT001-101 demonstrated that food increases the mean AUC and mean time over MIC (0.5 µg/mL) of 500 mg sulopenem etzadroxil dosed with 500 mg probenecid on Day 1 by 62% and 68%, respectively.

In IT001-105 we studied the bioavailability of sulopenem etzadroxil/probenecid in our planned commercial formulation of a bilayer tablet. The absolute bioavailability of the bilayer tablet was approximately 40% in a fasted state and 64% in the fed state. A graph of the sulopenem plasma concentrations in the patients in this trial is provided below.



A Phase 1 drug interaction study with itraconazole demonstrated no interaction. We plan to conduct an additional drug interaction study with valproic acid to support our NDAs. Other Phase 1 clinical trials may be added as the needs of the program dictate.

Sulopenem, IV Formulation

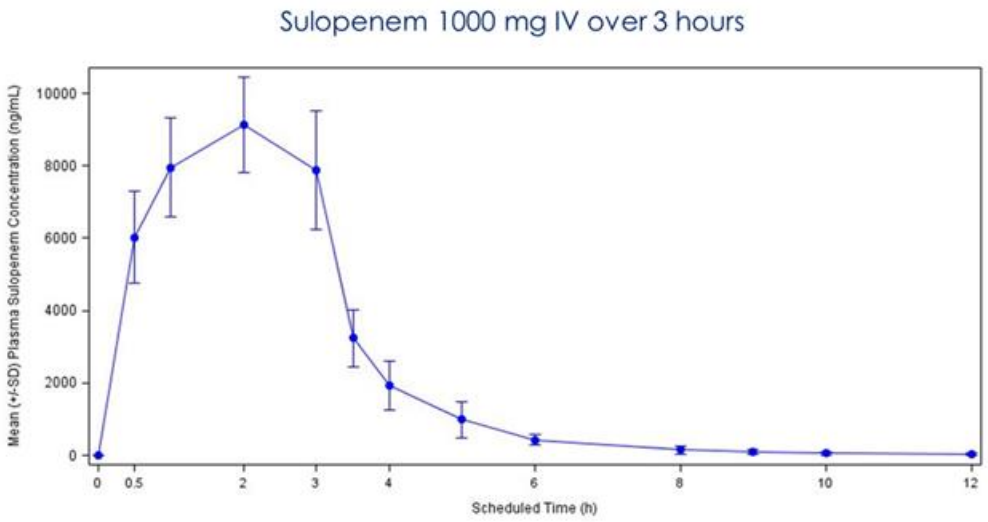
Doses of sulopenem up to 2800 mg as a single IV dose and 2000 mg BID, or twice daily, of sulopenem as IV over fourteen days were studied in three Phase 1 clinical trials in healthy adults, one study in patients with renal insufficiency in the United States and two Phase 1 clinical trials in Japan. Results from these pharmacokinetic studies with various IV doses of sulopenem delivered over various durations established dose proportionality among the regimens with regard to AUC and maximal plasma concentrations (Cmax). A representative analysis of pharmacokinetic parameters, a subset of study A1091001, is described in the table below.

	N	Dose (mg)	Infusion duration (h)	Cmax (µg/mL)	AUC 0-¥ (µg hr/mL)	T1/2 (h)	CLtotal (mL/min/kg)
Day 1	8	800	3	7.27	22.4	0.83	
	8	1200	1	32.5	42.3	1.04	
	8	1200	2.5	16.6	41.9	1.12	
Day 14	5	800	3	8.97	26.5	0.89	15.4
	6	1200	1	30.7	41.4	1.05	14.7
	6	1200	2.5	13.5	34.6	1.01	18.8

N = number of subjects; C_{max} = maximum plasma concentration; $AUC_{0-\infty}$ = area under the curve from the initiation of dosing extrapolated through infinite time; $T_{½}$ = half-life; CL_{total} = clearance (only measured on Day 14)

A single dose cross-over design study of 1000 mg of sulopenem infused over 3 hours was given to fasting healthy adults in our IT001-105 Phase 1 clinical trial. Pharmacokinetic parameters observed in this trial are described in the table below.

	N	Dose (mg)	Infusion duration (h)	Cmax (µg/mL)	AUC 0-¥ (µg hr/mL)	T1/2 (h)
Day 1	12	1000	3	9.15	28.9	1.65



Modeling and Dose Selection

Based on *in vitro* susceptibility data from surveillance studies, pharmacokinetics gathered from Phase 1 clinical trials, and population pharmacokinetic data from patients, we performed modeling to help choose the doses for the Phase 3 program. The MIC_{90} for all Enterobacteriaceae potentially involved in the target indications was 0.25 µg/mL and for the weighted distribution of pathogens most likely to be associated with the indication was 0.06 µg/mL. We have performed modeling both for the weighted distribution of MICs expected in the clinical trials as well as at a fixed MIC of 0.5 µg/mL. Data obtained from animal experiments confirmed that, similar to carbapenems and lower than that for other ß-lactams, the $\%T_{free}$ >MIC required for bacteriostasis is approximately 10–19%, depending on the dosing regimen; we have used 17% in our models. Based on the outputs from those models, the IV dose of sulopenem being studied in the ongoing Phase 3 clinical trials is 1000 mg sulopenem delivered over 3 hours once a day. The oral dose being studied is 500 mg of sulopenem etzadroxil given with 500 mg of probenecid in a single bilayer tablet twice daily.

Japanese Clinical Data

Pfizer's affiliate in Japan conducted extensive clinical development of sulopenem in over 1,450 patients in Phase 1 and Phase 2 clinical trials in Japan in patients with skin infections, respiratory tract infections, gynecologic infections, cUTI and intra-abdominal infections.

Phase 2 clinical trials conducted by Pfizer in Japan, 1991-1993

Study #	Description	Sulopenem Dose	Comparator	N
91-002	Multiple infections in: Internal medicine Surgery: includes cIAI Urology: pyelonephritis cystitis	250 mg IV BID 500 mg IV BID	None	108
92-002	Multiple infections in: Internal medicine Surgery: includes cIAI Urology: pyelonephritis cystitis	250 mg IV BID 500 mg IV BID	None	961
91-002 92-002	Population-Pharmacokinetics (only)	250 mg IV BID 500 mg IV BID	N/A	216
93-001	Respiratory Tract Infection	250 mg IV BID 500 mg IV BID	Cefotiam IV	75
93-002	cUTI	250 mg IV BID 500 mg IV BID	Imipenem IV	114
Total				**1474**

A treatment effect in small Phase 2 clinical trials was observed in a number of infections includingskin infections, respiratory tract infections, gynecologic infections and, most relevant to the targeted indications being pursued in our Phase 3 program, cUTI and cIAI. The data from these clinical trials may not be directly comparable to data from clinical trials that would be conducted today or the data that we anticipate from our Phase 3 program for a variety of reasons, including that the protocols were designed for different purposes and as a consequence had different enrollment and efficacy evaluation criteria. While these data are not required for approval of our intended indications, we believe these results support our decision to develop sulopenem for our targeted indications and informed our dose selection.

In 1993, Pfizer Japan conducted 93-002, a randomized clinical trial in subjects with cUTI, comparing 250 mg twice daily and 500 mg twice daily of sulopenem administered intravenously to an intravenously-delivered imipenem-cilastatin, also given twice daily.

The trial enrolled patients who were hospitalized, with an underlying disease of the urinary tract and with evidence of pyuria, measured by ≥ 5 WBC/hpf (white blood cells per high power field, a measure of inflammation in the urinary tract) at baseline. Study therapy was administered for five days and was open-label with respect to sulopenem versus the comparator but was blinded as to the sulopenem dose. Efficacy was assessed by the investigator based on subjective and objective criteria, as shown below.

The criteria for patient enrollment in the Phase 2 clinical trial 93-002 are different than those currently established by the FDA in guidelines for Phase 3 cUTI registrational trials published in 2015. In addition to an Intent-to-Treat (ITT) analysis, which includes all randomized patients, of the investigator's assessment of overall efficacy based on the original inclusion criteria, a *post hoc* analysis was also performed by Iterum of the investigator's assessment of overall efficacy in the population of patients that met enrollment criteria consistent with current FDA guidance, such as baseline urinalysis with >10 WBC/hpf and a urine culture which grew >10^5 susceptible organisms, as shown below. ITT analyses are performed in the population of all randomized patients. Success, as determined by the investigator and specified in the protocol, was judged for each patient based on resolution of symptoms, pyuria and bacteriuria.

Investigator Assessment of Overall Efficacy	**Sulopenem (CP 70,429) 250 mg BID IV n/N (%)**	**Sulopenem (CP 70,429) 500 mg BID IV n/N (%)**	**Comparator n/N (%)**
ITT			
Success	33/36 (91.7)	36/38 (94.7)	32/39 (82.1)
Failure	2/36 (5.6)	2/38 (5.3)	2/39 (5.1)
Indeterminant	1/36 (2.8)	0	5/39 (12.8)
Difference vs. comparator (95% CI)	9.6 (-6.6, 25.9)	12.7 (-2.1, 28.4)	
Clinically Evaluable using FDA inclusion criteria (*post hoc*)			
Success	19/20 (95.0)	22/22 (100.0)	16/16 (100.0)
Failure	1/20 (5.0)	0	0
Difference vs. comparator (95% CI)	-5.0 (-24.0, 15.3)	0 (-15.2, 19.8)	

One patient received a dose other than 250 mg or 500 mg IV BID.

The results of a subset analysis that included patients from clinical trials conducted in 1991 and 1992, 91-002 and 92-002, with a diagnosis that fit the FDA's definition of cIAIs are provided below, based on the investigator's assessment of clinical response at the end of therapy in the ITT and clinically evaluable populations. Success, as determined by the investigator and specified in the protocol, was judged for each patient based on resolution of cIAI signs and symptoms and improvement in relevant laboratory tests.

Investigator Assessment of Outcome	**Sulopenem (CP 70,429) 250 mg BID IV n/N (%)**	**Sulopenem (CP 70,429) 500 mg BID IV n/N (%)**
ITT		
Success	14/15 (93.3)	78/88 (88.6)
Failure	1/15 (6.7)	4/88 (4.5)
Indeterminant		6/88 (6.8)
Clinically Evaluable		
Success	14/15 (93.3)	77/81 (95.1)
Failure	1/15 (6.7)	4/81 (4.9)

Three patients received a dose other than 250 mg or 500 mg IV BID.

We used the data collected in these studies to inform the design of the cUTI regimens.

The results of a Phase 2 clinical trial conducted in 1993 in hospitalized patients with community acquired pneumonia (CAP), 93-001, are provided below, including the investigator's assessment of clinical response at the end of therapy in the ITT and clinically and bacteriologically evaluable populations with the bacteriologically evaluable population meaning the clinically evaluable patients who had a baseline pathogen and follow up microbiology data to allow an assessment of bacteriological efficacy. Success, as determined by the investigator and specified in the protocol, was judged for each patient based on resolution of the signs and symptoms of pneumonia, and improvement in radiologic findings and other relevant tests.

Investigator Response at End of Treatment	Sulopenem CP 70,429 250 mg BID IV n/N (%)	Sulopenem CP 70,429 500 mg BID IV n/N (%)	Comparator n/N (%)
ITT			
Success	19/26 (73.1)	17/23 (73.9)	22/25 (88.0)
Failure	4/26 (15.4)	3/23 (13.0)	2/25 (8.0)
Indeterminant	3/26 (11.5)	3/23 (13.0)	1/25 (4.0)
Difference vs. comparator (95% CI)	-14.9 (-36.7, 7.7)	-14.1 (-37.1, 8.8)	
Clinically Evaluable			
Success	18/20 (90.0)	15/17 (88.2)	20/20 (100.0)
Failure	2/20 (10.0)	2/17 (11.8)	
Difference vs. comparator (95% CI)	-10.0 (-30.4, 7.3)	-11.8 (-34.7, 5.8)	
Bacteriologically Evaluable			
Success	8/8 (100.0)	5/6 (83.3)	9/9 (100.0)
Failure	—	1/6 (16.7)	—
Difference vs. comparator (95% CI)	0.0 (-33.8, 31.2)	-16.7 (-57.6, 18.1)	

Phase 2 Clinical Trial with sulopenem and sulopenem etzadroxil

In 2009, Pfizer initiated a Phase 2, randomized, double-blind, double-dummy clinical trial in hospitalized patients with CAP comparing two regimens of IV sulopenem followed by sulopenem etzadroxil to ceftriaxone IV followed by amoxicillin-clavulanate. The sulopenem regimens were a single 600 mg IV dose of sulopenem followed by 1000 mg BID of sulopenem etzadroxil or a 600 mg of sulopenem for a minimum of four doses followed by 1000 mg BID of sulopenem etzadroxil. The clinical trial was terminated early for business reasons after 33 of 250 planned total patients were enrolled and treated. Clinical response rates at the test-of-cure visit (7–14 days after end of therapy) of the ITT patients were similar on each regimen (9/10, 9/11 and 7/12, on sulopenem single IV dose, sulopenem multidose IV and ceftriaxone, respectively). Treatment-emergent adverse events were reported in six subjects each in the sulopenem groups and eight subjects in the ceftriaxone group. The most common treatment-emergent adverse event was diarrhea, reported by a total of six subjects (two in each treatment group). Treatment related diarrhea was reported by one subject following sulopenem single dose IV, and by a further two subjects following ceftriaxone. There was one treatment-related serious adverse event in the ceftriaxone group. There were no deaths reported in this clinical trial.

Phase 3 Clinical Trials

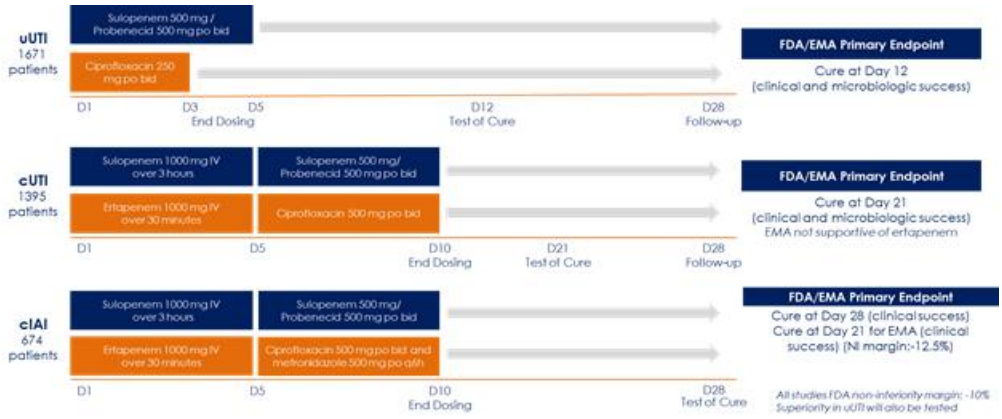
Based on FDA Guidance from February 2015 (Complicated Intra-Abdominal Infections: Developing Drugs for Treatment. Guidance for Industry; Complicated Urinary Tract Infections: Developing Drugs for Treatment. Guidance for Industry) and on recently conducted studies by other sponsors, we negotiated SPA agreements for cUTI, cIAI and uUTI. All three Phase 3 clinical trials were initiated in the third quarter of 2018, and completed enrollment by the end of 2019. Oral sulopenem alone is being studied for the treatment of outpatients with uUTI, while oral sulopenem and sulopenem are being studied for the treatment of cUTI. Oral sulopenem and sulopenem were also studied for the treatment of cIAI. A brief overview of the comparator agents, sample size, timing of efficacy assessments and duration of oral and IV dosing is provided in the graphic below. Non-inferiority in these clinical trials is defined by the lower limit of the confidence interval in the treatment difference of no more than -10%. The uUTI clinical trial is also testing for superiority in the subset of patients with ciprofloxacin resistant pathogens at baseline. An open-label noncomparative treatment study of oral ciprofloxacin 250 mg twice daily for three days in uUTI patients was conducted to help characterize certain sample size assumptions as well as enable study logistics for this Phase 3 clinical trial. Patients in the cUTI and cIAI clinical trials received five days of sulopenem IV or comparator and then stepped down to two to five additional days of oral treatment with either oral sulopenem or ciprofloxacin.

In the Phase 3 cIAI trial, clinical outcome at the test-of-cure visit was noted as cure for those patients who are alive, have resolution in signs and symptoms of the index infection and for whom no new antibiotics or interventions for treatment failure were required. The primary endpoint was clinical response on Day 28 in the micro-MITT population. The micro-MITT population consists of those randomized patients who received a dose of study drug and had a gram-negative organism isolated from their infection site. In this population, the difference in outcomes was 4.7% with a 95% confidence interval on that difference of -10.3% to 1.0%. Non-inferiority for the primary endpoint required that the lower limit of the difference in the outcome rates be >-10%:

	Sulopenem	Ertapenem	Difference (95% Confidence Interval)
Test of Cure			
microMITT	85.5%	90.2%	-4.7% (-10.3, 1.0)
MITT	87.2%	90.0%	-2.9% (- 7.7, 2.0)
Clinically Evaluable	93.5%	95.7%	-2.0% (-5.7, 1.7)
Microbiologically Evaluable	92.5%	95.5%	-3.0% (-7.5, 1.4)
End of Treatment			
microMITT	83.5%	85.3%	-1.8% (- 8.1, 4.5)
MITT	83.7%	85.4%	-1.7% (-7.1, 3.8)
Clinically Evaluable	89.4%	90.0%	-0.7% (-5.6, 4.3)
Microbiologically Evaluable	88.5%	88.9%	-0.4% (-6.3, 5.4)

In the uUTI and cUTI trials, clinical outcome at the test-of-cure visit will be noted as cure for patients who are alive and who demonstrate resolution of the symptoms of uUTI or cUTI, as applicable, present at trial entry (and no new symptoms) such that no new antibiotics are required, as well as the demonstration that the bacterial pathogen(s) found at trial entry are reduced to $<10^3$ CFU/mL on urine culture on Day 12 or Day 21, respectively. Topline results for the two remaining trials are expected around the end of the first quarter of 2020.

Patients with an organism resistant to ciprofloxacin in the cUTI and cIAI clinical trials were allowed to substitute amoxicillin-clavulanate for the stepdown oral therapy. Patients getting ciprofloxacin in the cIAI trial also received metronidazole. Patients who received oral sulopenem were encouraged, but not required, to dose with food.



Safety Profile of Oral Sulopenem and Sulopenem

Sulopenem is a thiopenem and a member of the class of ß-lactam antibiotics, a class from which numerous safe and well tolerated antibiotics have been available for over thirty years. Adverse event data collected as part of the Japanese Phase 2 development program with the IV formulation conducted by Pfizer provided preliminary insights into the safety profile for sulopenem, which will continue to be assessed with additional clinical trials. We view the clinical safety profile of sulopenem established by the Japanese data as also relevant and supportive of oral sulopenem because it metabolizes to the active metabolite, sulopenem, in plasma. A summary of the adverse event data from the Japanese program is provided below.

	Sulopenem				
	250 mg BID (N = 296)	**500 mg BID (N = 867)**	**Miscellaneous* (N = 247)**	**Comparators (N = 64)**	**Total (N = 1474)**
No. of patients who experienced at least one:					
Adverse Event	14 (4.7)	35 (4.0)	1 (0.4)	3 (4.7)	53 (3.6)
Drug-Related Adverse Event	9 (3.0)	22 (2.5)	1 (0.4)	3 (4.7)	35 (2.4)
Serious Adverse Event	2 (0.7)	1 (0.1)	—	1 (1.6)	4 (0.3)
Drug-Related Serious Adverse Event	1 (0.3)	—	—	1 (1.6)	2 (0.1)
SAE Leading to Death	2 (0.7)	1 (0.1)	—	1 (1.6)	4 (0.3)

	Sulopenem				
	250 mg BID (N = 296)	500 mg BID (N = 867)	Miscellaneous* (N = 247)	Comparators (N = 64)	Total (N = 1474)
AE Leading to Premature Discontinuation of Study Drug	8 (2.7)	16 (1.8)	—	2 (3.1)	26 (1.8)
SAE Leading to Premature Discontinuation of Study Drug	1 (0.3)	—	—	—	1 (0.1)

* Miscellaneous doses include patients receiving a total daily dose of 250 mg, 750 mg, 1500 mg or 2000 mg, including patients receiving a single dose of sulopenem in the population PK sub-study.

Common adverse events occurring in more than one patient on a sulopenem regimen included diarrhea (0.7%), pyrexia (0.5%) and rash (1.0%). The most common adverse event leading to discontinuation was rash (0.7%). Clinically significant laboratory test abnormalities were infrequent. Elevations in serum aminotransferases occurred in approximately 4% of patients.

Data is also available for the oral formulation collected in healthy volunteers in the Phase 1 program conducted by Pfizer and Iterum that is consistent with the adverse event profile observed with the IV formulation. One additional adverse event of interest identified with the oral prodrug, as further assessed in detail in clinical trial IT001-101, is loose stool/diarrhea, which was considered of mild severity and self-limited, as seen with other broad spectrum oral antibiotics with activity against the anaerobic flora of the gastrointestinal tract. During the seven-day dosing interval, the incidence of diarrhea, defined as having three or more episodes of loose stool in one day or having two or more episodes of loose stool per day for two consecutive days, peaked at 13% on Day 3 and fell to 2% by Day 7, with no patient discontinuing their dosing due to this event. For patients who took their dose with food, the peak incidence was 9%, dropping again to 3% by Day 4, similar to placebo. Some patients also identified a mild change in the odor of their urine after dosing with either the oral or IV formulations, as can be seen with other ß-lactam antibiotics.

In the cIAI trial, among 668 treated patients, treatment-related adverse events were observed in 6.0% and 5.1% of patients on sulopenem and ertapenem, respectively, with the most commonly reported drug-related adverse event being diarrhea, which was observed in 4.5% and 2.4% of patients on sulopenem and ertapenem, respectively. Discontinuations from treatment were uncommon for both regimens, occurring in 1.5% of patients on sulopenem and 2.1% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 7.5% of patients on sulopenem and 3.6% of patients on ertapenem.

We have received a waiver from the FDA for the requirement of performing a thorough QT interval study given the lack both of any significant preclinical findings and signals in Phase 1 clinical trials during which intensive electrocardiogram monitoring was performed. The EMA in written scientific advice also agreed that a QT interval study is not warranted. A preclinical study of the hydrolysis product of etzadroxil (2-ethylbutyric acid) has been performed in which no effect on plasma carnitine in rats was identified, while a significant effect of a different prodrug moiety, pivoxil, was observed. No reports of seizures, seen with some members of the carbapenem class, were noted in preclinical studies or clinical trials.

Pfizer License Agreement

In November 2015, we and our wholly owned subsidiary, Iterum Therapeutics International Limited, entered into a license agreement with Pfizer (the Pfizer License), pursuant to which we acquired from Pfizer an exclusive, royalty-bearing license under certain patent rights and know-how to develop, manufacture and commercialize sulopenem and related compounds, including, among others, sulopenem etzadroxil and three other sulopenem prodrugs, globally for the treatment, diagnosis and prevention of infectious diseases and infections in humans. The licensed patents include two U.S. patents, one of which covers the composition of matter of sulopenem etzadroxil, one patent in Japan, one patent in Hong Kong and one patent in Mexico. None of the licensed patents cover the IV formulation of sulopenem. All patents directed to the compound sulopenem expired prior to us entering into the Pfizer License. Pursuant to the Pfizer License, our exclusive license from Pfizer includes certain know-how, data and regulatory documents that will support the development of sulopenem. We have the right to grant development or commercialization sublicenses to third parties, provided that we (1) obtain Pfizer's prior written consent in connection with such sublicense, (2) enter into a written sublicense agreement consistent with the terms and conditions of the Pfizer License and (3) include Pfizer as a third-party beneficiary under such sublicense. As between Pfizer and us, we own all right, title and interest in any intellectual property rights that are developed by us or our sublicensees in connection with the Pfizer License.

Under the Pfizer License, we have sole responsibility for and control over the development, regulatory approval, manufacture and commercialization of licensed products worldwide, including bearing all costs and expenses associated therewith. We are obligated to use commercially reasonable efforts to develop and seek regulatory approval for one licensed product in the United States and in at least one country out of any of France, Germany, Italy, Japan, Spain or the United Kingdom (Major Market Countries) and, if deemed appropriate by us in our exercise of commercially reasonable efforts, for a second licensed product in the United States or at least one Major Market Country. In addition, we must use commercially reasonable efforts to commercialize a licensed product in the United States and each Major Market Country in which we have received regulatory approval for such product.

Under the Pfizer License, we have paid Pfizer a one-time nonrefundable upfront fee of $5.0 million and a total of $15.0 million in clinical milestones based on first patient dosed in our Phase 3 clinical trials with sulopenem etzadroxil and sulopenem IV and are obligated to pay Pfizer potential future regulatory milestone payments, as well as potential sales milestones upon achievement of net sales ranging from $250.0 million to $1.0 billion for each product type (sulopenem etzadroxil and other prodrugs, and sulopenem and other non-prodrugs). We are obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage of marginal net sales of each licensed product. Pfizer also received 381,922 of our Series A preferred shares (which converted to ordinary shares in connection with our initial public offering) at a value of $15.71 per share as additional payment for the licensed rights. In addition, if we sublicense or assign any of our rights to any licensed products to a third party, and we receive in connection with such transaction a threshold amount of at least a low nine figure dollar amount over a specified period of time, we will be obligated to pay Pfizer an additional one-time payment of a low eight figure dollar amount.

At our cost and expense, we are responsible for the prosecution and maintenance of the licensed patents worldwide, using specific legal counsel in various jurisdictions as set forth in the Pfizer License. If we elect to forgo prosecution or maintenance of a licensed patent, we must notify Pfizer and Pfizer has the right to continue prosecution and maintenance of such licensed patent and the exclusive license granted to us under such licensed patent will become a non-exclusive and non-sublicensable license. Subject to certain consultation rights granted to Pfizer, we have the first right, but not the obligation, to enforce the licensed patents at our cost and expense. If we elect to enforce any licensed patent, we may not enter into a settlement agreement that would: (1) adversely affect the validity, enforceability or scope of any of the licensed patents, (2) give rise to any liability for Pfizer, (3) admit non-infringement of any of the licensed patents or (4) otherwise impair Pfizer's rights in any of the licensed patents or licensed know-how without the prior written consent of Pfizer.

The Pfizer License continues in effect until the expiration of all royalty terms thereunder, unless earlier terminated. Upon such expiration, the Pfizer License shall become non-exclusive, fully-paid, royalty free, perpetual and irrevocable. The royalty term for each licensed product in each country begins as of the first commercial sale of such licensed product in such country and lasts until the later of (1) the expiration of the applicable licensed patents in such country, (2) the expiration of regulatory or data exclusivity for such licensed product in such country and (3) fifteen years after the first commercial sale of such licensed product in such country. Pursuant to the terms of the Pfizer License, each party has the right to terminate the Pfizer License upon the other party's (1) material breach of the Pfizer License that remains uncured after 60 days (or, if the breach cannot be cured in 60 days, up to 150 days) of receipt of notice or (2) insolvency. In addition, we have the unilateral right to terminate the Pfizer License for convenience by providing 90 days' written notice to Pfizer.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining rights in patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture and any other inventions that are commercially important to the development of our business. However, we do not currently own any patents and rely heavily on the Pfizer License for intellectual property rights that are important or necessary for the development of oral sulopenem and the IV formulation of sulopenem. In addition, we do not license any patent rights that cover the IV formulation of sulopenem and all patent rights covering the compound sulopenem expired prior to us entering into the Pfizer License. We also rely, in some circumstances, on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will significantly depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology and inventions and know-how related to our business, defend and enforce our in-licensed patents and patents we may own in the future, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and other proprietary rights of third parties. We also rely on know-how and continuing technological innovation to develop and maintain our proprietary position.

Intellectual Property Relating to Oral Sulopenem

As noted above, our patent portfolio for sulopenem contains one exclusively licensed U.S. patent from Pfizer directed to composition of matter of sulopenem etzadroxil, which is projected to expire in 2029, subject to potential extension under the Hatch-Waxman Act to 2034 and three exclusively licensed foreign patents from Pfizer also related to oral sulopenem. Our patent portfolio also contains two U.S. and International patent applications, one addressing the effect of probenecid on the plasma concentrations of sulopenem after multi-dosing and the second related to a method of preparing a bilayer tablet composed of sulopenem etzadroxil and probenecid which resulted in an increase in the amount of sulopenem in the blood relative to dosing each agent in a separate formulation. Any U.S. or foreign patents issuing from the pending applications is projected to expire in 2039, excluding any additional term for patent adjustments or patent term extensions. The FDA has designated sulopenem and oral sulopenem as QIDPs for the indications of uUTI, cUTI and cIAI as well as community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous

formulations has also been granted. QIDP status makes sulopenem eligible to benefit from certain incentives for the development of new antibiotics provided under the GAIN Act. Further, QIDP status could add five years to any other regulatory exclusivity period that may be granted. QIDP status for other indications is also possible given the coverage of gram-negative and gram-positive bacteria by sulopenem, pending submission of additional documentation and acceptance by the FDA. Patent term adjustments or patent term extensions could result in later expiration dates. Fast track status provides an opportunity for more frequent meetings with the FDA, more frequent written communication related to the clinical trials, eligibility for accelerated approval and priority review and the potential for a rolling review.

Patent Term and Patent Term Extensions

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug, biological product or medical device approved pursuant to a pre-market approval may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug are extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug.

Trade Secrets

We rely, in some circumstances, on trade secrets to protect our unpatented technology. However, trade secrets can be difficult to protect. We seek to protect our trade secrets and proprietary technology and processes, in part, by entering into non-disclosure and confidentiality agreements with our employees, consultants, scientific advisors, suppliers, contractors and other third parties. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and our trade secrets and other proprietary information may be disclosed. We may not have adequate remedies for any breach and could lose our trade secrets and other proprietary information through such a breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting trade secrets, know-how and inventions. For more information regarding the risks related to our intellectual property, see the section titled "Risk Factors—Risks Related to our Intellectual Property."

Competition

The pharmaceutical industry is characterized by intense competition and rapid innovation. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical companies and generic drug companies. Many of our potential competitors have greater financial, technical and human resources than we do, as well as greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our potential competitors may be more successful than us in obtaining FDA approved drugs and achieving widespread market acceptance. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render our product candidates non-competitive or obsolete.

We believe the key competitive factors that will affect the development and commercial success of oral sulopenem and sulopenem, if approved, will be efficacy, coverage of drug-resistant strains of bacteria, safety and tolerability profile, reliability, convenience of oral dosing, price, availability of reimbursement from governmental and other third-party payors and susceptibility to drug resistance.

If approved, oral sulopenem could compete with several oral antibiotics currently in clinical development, includinggepotidacin from GlaxoSmithKline, tebipenem pivoxil from Spero Therapeutics, Inc., delafloxacin from Melinta Therapeutics, Inc., pivmecillinam from Utility Therapeutics Limited, and ETX0282CPDP (a novel ß-lactamase inhibitor combined with cefpodoxime proxetil) from Entasis Therapeutics Holdings Inc.

We also expect that oral sulopenem, if approved, would compete with future and current generic versions of marketed oral antibiotics such as levofloxacin, ciprofloxacin, nitrofurantoin, fosfomycin, amoxicillin-clavulanate, cephalexin and trimethoprim-

sulfamethoxazole. If approved, we believe that oral sulopenem would compete effectively against these compounds on the basis of sulopenem's potential:

- broad range of activity against a wide variety of resistant and MDR gram-negative bacteria;
- low probability of drug resistance;
- favorable safety and tolerability profile;
- convenient oral dosing regimen and opportunity to step down from IV-administered therapy; and
- use as a monotherapy treatment for resistant and MDR gram-negative infections.

If approved, sulopenem would compete with several IV-administered product candidates marketed for the treatment of gram-negative infections,including Avycaz from Allergan plc and Pfizer, Vabomere from Melinta Therapeutics, Inc., Zerbaxa from Merck & Co., Zemdri from Cipla, Xerava from Tetraphase Pharmaceuticals, Inc., Recarbrio from Merck & Co, and recently, Fetroja from Shionogi & Co., Ltd. In addition, Nabriva Therapeutics plc's Contepo is an IV-administered product candidate in late-stage clinical development intended to treat gram-negative infections and Allecra Therapeutics recently announced that its IV administered product candidate cefepime-enmetazobactam met the EMA and FDA primary endpoint in its Phase 3 clinical trial for the treatment of cUTIs.

If approved, we believe that sulopenem would compete effectively and potentially occupy an earlier place in treatment against these compounds on the basis of sulopenem's potential, including that sulopenem:

- allows physicians to stay in the same molecule with stepdown therapy to oral sulopenem;
- has a convenient once a day dosing over a three-hour infusion period;
- has a broad spectrum activity against a wide variety of resistant and MDR gram-negative bacteria;
- has a low probability of drug resistance; and
- has a favorable safety and tolerability profile.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries, extensively regulate, among other things, the research, development, clinical trials, testing, manufacture, including any manufacturing changes, authorization, pharmacovigilance, adverse event reporting, recalls, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, import and export of pharmaceutical products and product candidates such as those we are developing. The processes for obtaining regulatory approvals in the United States and in other countries, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources.

United States Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (FDCA) and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. The failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil and/or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with good laboratory practices (GLP) regulations;
- submission to the FDA of an investigational new drug (IND) application which must become effective before human clinical trials may begin;
- approval by an independent institutional review board (IRB) at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices (GCPs) to establish the safety and efficacy of the proposed drug product for each indication;

- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices (cGMP), and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of clinical data;
- payment of user fees and securing FDA review and approval of the NDA; and
- commitment to comply with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy (REMS), and the potential requirement to conduct post-approval studies.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. Preclinical tests intended for submission to the FDA to support the safety of a product candidate must be conducted in compliance with GLP regulations and the United States Department of Agriculture's Animal Welfare Act. A drug sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical trials, nonclinical studies, and/or CMC. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

Clinical Trials

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial along with the requirement to ensure that the data and results reported from the clinical trials are credible and accurate. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the criteria for determining subject eligibility, the dosing plan, the parameters to be used in monitoring safety, the procedure for timely reporting of adverse events, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about, and results from, certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their *www.clinicaltrials.gov* website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness. During Phase 1 clinical trials, sufficient information about the investigational drug's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.

Phase 2: The drug is administered to a larger, but still limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted indications and to determine dosage tolerance and optimal dosage. Phase 2 clinical trials are typically well-controlled and closely monitored.

Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product. Phase 3 clinical trials usually involve a larger number of participants than a Phase 2 clinical trial.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Results from one trial may not be predictive of results from subsequent trials. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Information about clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on its ClinicalTrials.gov website. Similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries, as well.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

On December 13, 2016, the 21st Century Cures Act established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2020 is $2,942,965 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2020 is $325,424. On January 14, 2020, FDA granted us a small business waiver of the application fee in respect of our NDA for IV sulopenem based on its determination that we meet the statutory requirements of the FDCA. The waiver is contingent on the marketing application for IV sulopenem being received by FDA within one year from the grant date. Under the Prescription Drug User Fee Act (PDUFA) guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision. Furthermore, the FDA is not required to complete its review within the established ten-month timeframe and may extend the review process by issuing requests for additional information or clarification.

In addition, under the Pediatric Research Equity Act of 2003, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirements.

The FDA also may require submission of a REMS plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facilities in which it is manufactured, processed, packaged or held meet standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCP.

The FDA generally accepts data from foreign clinical trials in support of an NDA if the trials were conducted under an IND. If a foreign clinical trial is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA if the study was conducted in accordance with GCPs and the FDA is able to validate the data through an on-site inspection, if deemed necessary. The testing and approval process for an NDA requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from preclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met before the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Special FDA Expedited Review and Approval Programs

The FDA has various programs that are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need, or if the drug qualifies as a QIDP under the GAIN Act. We obtained a QIDP designation for sulopenem and oral sulopenem for the indications of cUTI, uUTI and cIAI in 2016 and 2017, respectively, and the indications of community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease in 2019 and fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

The FDA may give a priority review designation to drugs that offer major advances in treatment for a serious condition or provide a treatment where no adequate therapy exists. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. These six and ten month review periods are measured from the "filing" date for NDAs for new molecular entities. The FDA will automatically give a priority review designation for the first application submitted in respect of a product for which a QIDP designation was granted, such as sulopenem and oral sulopenem.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product label, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program user fee requirements for any marketed products, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

The FDA strictly regulates the marketing, labeling, advertising and promotion of drug products that are placed on the market. A product cannot be commercially promoted before it is approved, and approved drugs may generally be promoted only for their approved indications. Promotional claims must also be consistent with the product's FDA-approved label, including claims related to safety and effectiveness. The FDA and other federal agencies also closely regulate the promotion of drugs in specific contexts such as direct-to-consumer advertising, industry-sponsored scientific and education activities, and promotional activities involving the Internet and social media.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences of regulatory non-compliance include, among other things:

- restrictions on, or suspensions of, the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- interruption of production processes, including the shutdown of manufacturing facilities or production lines or the imposition of new manufacturing requirements;
- fines, warning letters or other enforcement letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (PDMA), which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Exclusivity and Approval of Competing Products

Hatch-Waxman Exclusivity

Market and data exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the activity of the drug substance. We believe that our product candidates are new chemical entities. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA), or a 505(b)(2) NDA, submitted by another company that references the previously approved drug. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application or supplement. Three-year exclusivity may be awarded for changes to a previously approved drug product, such as new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Qualified Infectious Disease Product Exclusivity

Under the GAIN Act, the FDA may designate a product as a QIDP. In order to receive this designation, a drug must qualify as an antibiotic or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by either (i) an antibiotic or antifungal resistant pathogen, including novel or emerging infectious pathogens, or (ii) a so-called “qualifying pathogen” found on a list of potentially dangerous, drug-resistant organisms established and maintained by the FDA. A sponsor must request such designation before submitting a marketing application. We obtained QIDP designation for sulopenem and oral sulopenem for the indications of cUTI, uUTI and cIAI in 2016 and 2017, respectively, as well as for the indications of community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease in 2019. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted.

Upon approving an application for a QIDP, the FDA will extend by an additional five years any regulatory exclusivity period awarded, such as a five-year exclusivity period awarded for a new molecular entity. This extension is in addition to any pediatric exclusivity extension awarded, and the extension will be awarded only to a drug first approved on or after the date of enactment.

The GAIN Act provisions prohibit the grant of an exclusivity extension where the application is a supplement to an application for which an extension is in effect or has expired, is a subsequent application for a specified change to an approved product or is an application for a product that does not meet the definition of QIDP based on the uses for which it is ultimately approved.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA or biologics license application sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data does not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to a variety of regulations governing clinical trials and commercial sales and distribution of our products outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of other countries or economic areas, such as the European Union, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product authorization, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new legislation aims at simplifying and streamlining the approval of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one EU Member State will only be required to submit a single application for approval of a clinical trial to a reporting EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials. As of January 1, 2020, the website of the European Commission reported that the implementation of the new Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure is compulsory for medicinal products produced by biotechnology or those medicinal products containing new active substances for specific indications such as the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and designated orphan medicines, and optional for other medicines which are highly innovative. Under the centralized procedure, a marketing application is submitted to the EMA where it will be evaluated by the Committee for Medicinal Products for Human Use and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all European Union member states within 67 days of receipt of the opinion. The initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period. The decentralized procedure provides for approval by one or more "concerned" member states based on an assessment of an application performed by one member state, known as the "reference" member state. Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the United Kingdom will not accept high regulatory alignment with the European Union.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to

products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation (GDPR) which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pharmaceutical Coverage and Reimbursement

Sales of drug products depend, in part, on the availability and extent of coverage and reimbursement by third-party payors, such as government health programs, including Medicare and Medicaid, commercial insurance and managed healthcare organizations. Obtaining coverage and reimbursement approval for a drug product from third-party payors is a time-consuming and costly process that can require the provision of supporting scientific, clinical and cost effectiveness data for the use of drug products to the payor. There may be significant delays in obtaining such coverage and reimbursement for newly approved drug products, and coverage may be more limited than the purposes for which the drug product is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug product will be paid for in all cases or at a rate that covers operating costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Reimbursement rates may vary according to the use of the drug product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drug products and may be incorporated into existing payments for other services.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved drug products. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but also have their own methods and approval process apart from Medicare coverage and reimbursement determinations. It is difficult to predict what third-party payors will decide with respect to coverage and reimbursement for new drug products. An inability to promptly obtain coverage and adequate reimbursement rates from third-party payors for any approved drug products could have a material adverse effect on a pharmaceutical manufacturer's operating results, ability to raise capital needed to commercialize drug products and overall financial condition.

Reimbursement may impact the demand for, and/or the price of, any drug product which obtains marketing approval. Even if coverage is obtained for a given drug product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with those medications. Patients are unlikely to use a drug product, and physicians may be less likely to prescribe a drug product, unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of the drug product. Therefore, coverage and adequate reimbursement is critical to new drug product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

The containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement, and requirements for substitution of generic drug products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a pharmaceutical manufacturer's net revenue and results.

In addition, it is expected that the increased emphasis on managed care and cost containment measures in the United States by third-party payors will continue and place further pressure on pharmaceutical pricing and coverage. Coverage policies and third-party

reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more drug products that gain regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, in the EU, the sole legal instrument at the EU level governing the pricing and reimbursement of medicinal products is Council Directive 89/105/EEC (the Price Transparency Directive). The aim of the Price Transparency Directive is to ensure that pricing and reimbursement mechanisms established in the EU Member States are transparent and objective, do not hinder the free movement of and trade in medicinal products in the EU, and do not hinder, prevent or distort competition on the market. The Price Transparency Directive does not provide any guidance concerning the specific criteria on the basis of which pricing and reimbursement decisions are to be made in individual EU Member States, nor does it have any direct consequence for pricing or reimbursement levels in individual EU Member States. The EU Member States are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement, and to control the prices and/or reimbursement levels of medicinal products for human use. An EU Member State may approve a specific price or level of reimbursement for the medicinal product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the medicinal product on the market, including volume-based arrangements, caps and reference pricing mechanisms.

Health Technology Assessment (HTA) of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including the United Kingdom, France, Germany, Ireland, Italy and Sweden. The HTA process in the EU Member States is governed by the national laws of these countries. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact, and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product vary between EU Member States. A negative HTA of one of our products by a leading and recognized HTA body, such as the National Institute for Health and Care Excellence in the United Kingdom, could not only undermine our ability to obtain reimbursement for such product in the EU Member State in which such negative assessment was issued, but also in other EU Member States. For example, EU Member States that have not yet developed HTA mechanisms could rely to some extent on the HTA performed in countries with a developed HTA framework, such as the United Kingdom, when adopting decisions concerning the pricing and reimbursement of a specific medicinal product.

Other Healthcare Laws

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug product candidates which obtain marketing approval. In addition to FDA restrictions on marketing of pharmaceutical products, pharmaceutical manufacturers are exposed, directly, or indirectly, through customers, to broadly applicable fraud and abuse and other healthcare laws and regulations that may affect the business or financial arrangements and relationships through which a pharmaceutical manufacturer can market, sell and distribute drug products. Such laws include, without limitation:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, in return for either the referral of an individual, or the purchase, leasing, furnishing or arranging for the purchase, lease or order of a good, facility, item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other hand. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, (ACA) amended the intent requirement of the federal Anti-Kickback Statute, such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it;
- the federal false claims and civil monetary penalty laws, including the federal False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other government payors that are false or fraudulent. In addition, the ACA provides, and recent government cases against pharmaceutical and medical device manufacturers support the view, that federal Anti-Kickback Statute violations and certain marketing practices, including off-label promotion, may implicate the federal False Claims Act. Further, pharmaceutical manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. Criminal prosecution is also possible for making or presenting a false, fictitious or fraudulent claim to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which, among other things, imposes criminal liability for executing or attempting to execute a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and creates federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statements or representations, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry in connection with the delivery of, or payment for, benefits, items or services;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act of 2009 (HITECH) and its implementing regulations, which impose certain requirements relating to the privacy, security, transmission and breach reporting of individually identifiable health information upon certain health plans, healthcare clearinghouses and healthcare providers and their respective business associates that perform services for them that involve individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- the federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act," and its implementing regulations, which require certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services (HHS) information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, that may impose similar or more prohibitive restrictions, and may apply to items or services reimbursed by non-governmental third-party payors, including private insurers; and
- state and foreign laws that require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or to track and report gifts, compensation and other remuneration provided to physicians and other healthcare providers, state and local laws that require the registration of pharmaceutical sales representatives, and other federal, state and foreign laws that govern the privacy and security of health information or personally identifiable information in certain circumstances, including state health information privacy and data breach notification laws which govern the collection, use, disclosure, and protection of health-related and other personal information, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus requiring additional compliance efforts.

Because of the breadth of these laws and the narrowness of their exceptions and safe harbors, it is possible that business activities can be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry.

Ensuring that business arrangements with third parties comply with applicable healthcare laws and regulations is costly and time consuming. If business operations are found to be in violation of any of the laws described above or any other applicable governmental regulations a pharmaceutical manufacturer may be subject to penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from governmental funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, additional reporting obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of operations, any of which could adversely affect a pharmaceutical manufacturer's ability to operate its business and the results of its operations.

Healthcare Reform

In the United States, there have been, and continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect the future results of pharmaceutical manufacturers' operations. In particular, there have been and continue to be a number of initiatives at the federal and state levels that seek to reduce healthcare costs. Most recently, ACA, which was enacted in March 2010, includes measures to significantly change the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, of greatest importance to the pharmaceutical and biotechnology industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price (AMP);
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing on January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health program;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services (CMS) to test innovative payment and service delivery models to lower Medicare and Medicaid spending; and
- implementation of the federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act."

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealedthe "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated , effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to replace elements of the ACA during the next Congressional session.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review

the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products.

Further, there has been heightened governmental scrutiny in the United States of the manner in which manufacturers set prices for their marketed products in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. These new laws and initiatives may result in additional reductions in Medicare and other healthcare funding, as well as limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures, all of which could have a material adverse effect on our future customers and accordingly, our financial operations.

Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. Under this blueprint for action, the Trump administration indicated that HHS will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

HHS has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. Although a number of these, and other potential proposals, will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. In addition, on December 23, 2019, the Trump Administration published a proposed rulemaking that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants would be required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, the FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

In addition, the CMS has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization (PA) and step therapy (ST) for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" while a definition of "price concession" in the regulations. It is unclear whether these proposed changes we be accepted, and if so, what effect such changes will have on our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

In addition , on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. On December 18, 2019, that court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On January 21, 2020, the U.S. Supreme Court declined to review this decision on an expedited basis. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on

certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Commercialization Strategy and Organization

Given our stage of development, we have not yet established a commercial organization or distribution capabilities. If approved, we intend to commercialize our sulopenem program in the United States with a commercial partner and/or on our own with a targeted sales force across the community and hospital settings.

Prior to receiving approval, we plan to establish a health resources group to familiarize doctors in the community setting with the rising rate of resistance of pathogens to the current oral therapies for UTI. If approved, we will direct our health resources group to promote antibiotic stewardship, particularly of oral sulopenem, by educating physicians in the community setting about patients for whom sulopenem may be an appropriate treatment option. In the hospital setting, we believe our sulopenem program will support stewardship efforts in the hospital focused on reduction in treatment length-of-stay by providing a safe and effective oral therapy that can be completed in an outpatient setting. Our health resources group will also work with hospitals, provider organizations and payors to demonstrate that the use of sulopenem may reduce the length of a patients' hospital stay or avoid hospital admission altogether, which we believe would lower the total cost of treatment of cUTI, and in some cases uUTI when inappropriate therapy leads to higher hospitalization rates or poor clinical outcomes for elevated risk patients. In addition, we expect that our health resources group will also work with doctors in the infectious disease field to answer questions regarding sulopenem's clinical results and its pharmacokinetic profile, conduct medical education events regarding the emerging science and build awareness of sulopenem.

If the FDA approves oral sulopenem and sulopenem, we plan to build a commercial infrastructure to launch both product candidates in the United States. We expect that our commercial infrastructure, led by highly-experienced management personnel, would be comprised of a targeted sales force, an internal marketing and health resources group, as well as a managed markets group focused on reimbursement activities with third-party payors and a specialty distribution team. We also plan to have in place a patient and healthcare practitioner support group to assist with information requests, reimbursement logistics and assistance, and provide educational materials where appropriate. To ensure successful execution of these critical activities, we may need to hire personnel to fill some of these functions in advance of the anticipated approval date. Further, if we choose to engage with a commercial partner in the United States, we would expect to reach a broader percentage of the market for sulopenem.

We expect to direct our sales and marketing efforts toward the community and hospital practitioner settings that account for a substantial majority of the potential market for oral sulopenem and sulopenem across geographies with the highest prevalence of bacterial resistance to fluoroquinolones. Based on an ongoing market survey data of outpatient urine cultures of Enterobacteriaceae and quinolone resistance by zip code, we estimate that our initial sales force could successfully target key customers including top hospitals and emergency room clinics, as well as specialty and primary care practices in the community setting. As access for, and awareness of, our sulopenem program increases, we would plan to broaden our target audience and geography by increasing the number of sales representatives to capture a larger percentage of the market.

We are focusing our initial commercial efforts on the U.S. market, which we believe represents the largest market opportunity for our sulopenem program. We are currently evaluating our commercialization strategy outside the United States and believe that Europe and Asia represent significant opportunities because of rising rates of ESBL and quinolone resistance in these geographies, which in many countries exceeds the United States' resistance rate.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of any of our product candidates. We currently rely on four third-party contract manufacturers for all of our required raw materials, drug substance, and finished drug product for our preclinical research and clinical trials. As of February 29, 2020, we had a 9-person team dedicated to managing the relationships with these manufacturers and the manufacturing process. Due to the complex and critical nature of drug manufacturing, we have employed a dual sourcing strategy in order to register two suppliers and validate at least one supplier for both sulopenem APIs at the time of submitting our NDAs, with each supplier capable of producing commercial scale quantities under cGMP conditions. We also intend to have a third-party manufacturer to produce the oral sulopenem bilayer tablets. In the future, given the importance of our oral formulation, we plan to pursue additional sources to manufacture tablets. We plan to use another third party to manufacture the IV vials. Potential additional sources to manufacture IV vials have also been identified.

Employees

As of February 29, 2020, we had 44 employees, including a total of nine employees with M.D., Pharm.D. or Ph.D. degrees. 32 employees were primarily engaged in research and development activities, with the rest providing administrative, business and operations support. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our employee relations to be good.

Our Corporate Information

We were incorporated under the laws of the Republic of Ireland in June 2015 as a limited company and re-registered as a public limited company on March 20, 2018. Our principal executive offices are located at Block 2 Floor 3, Harcourt Centre, Harcourt Street, Dublin 2, Ireland, and our telephone number is (+353) 1 903-8920.

Available Information

We maintain a website with the address www.iterumtx.com. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934 (the Exchange Act). We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. You can review our electronically filed reports, proxy and information statements and other information that we file with the SEC on the SEC's web site at http://www.sec.gov. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K.

Item 1A. Risk Factors.

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K and in other documents that we file with the SEC, in evaluating our company and our business. Investing in our ordinary shares involves a high degree of risk. If any of the events described in the following Risk Factors and the risks described elsewhere in this Annual Report on Form 10-K actually occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our ordinary shares could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Position and Capital Requirements

We have incurred net losses in each year since our inception and anticipate that we will continue to incur significant losses unless we successfully commercialize our sulopenem program.

We are a clinical-stage pharmaceutical company with a limited operating history. We have not generated any product revenue and have incurred net losses in each year since our inception in 2015. As of December 31, 2019, we had an accumulated deficit of $234.9 million. Our product candidates, oral sulopenem and sulopenem (together, the sulopenem program), are in clinical development, and have not been approved for sale and we may never have our product candidates approved for commercialization. We have financed our operations to date primarily with proceeds from the sale of preferred shares and ordinary shares, through a private placement(the Private Placement) of our ordinary shares, being the subscription for ordinary shares by our supplier and, more recently, through a private placement pursuant to which our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), sold units consisting of (i) 6.500% Exchangeable Senior Subordinated Notes due 2025 (Exchangeable Notes); and (ii) Limited Recourse Royalty-Linked Subordinated Notes (RLNs), to certain existing and new investors. In April 2018, we entered into a secured credit facility with Silicon Valley Bank (SVB) and made an initial drawdown of $15.0 million. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical and clinical development, for our sulopenem program.

We expect to continue to incur significant expenses and increasing operating losses as we conduct our ongoing and planned clinical trials of oral sulopenem and sulopenem, seek marketing approval for such product candidates in target territories if clinical trials are successful, and pursue the development of our sulopenem program in additional indications through preclinical and clinical development. Our expenses will also increase substantially if and as we:

- conduct additional clinical trials for oral sulopenem and sulopenem, which include our planned Phase 1 clinical trials related to pediatric indications;
- initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize oral sulopenem and sulopenem in the United States if we obtain marketing approval from the U.S. Food and Drug Administration (FDA) and we choose to commercialize directly in the United States;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of oral sulopenem and sulopenem, if we obtain marketing approval;
- pursue the development of our sulopenem program in additional indications;
- maintain, expand, defend and protect our intellectual property portfolio;
- hire additional clinical, scientific and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our ongoing transition to a public reporting company; and
- acquire or in-license other product candidates or technologies.

We will require additional capital to fund our operations, and there is substantial doubt about our ability to continue as a going concern for a period of one year from the date of this Annual Report on Form 10-K. If we fail to obtain financing when needed or on acceptable terms, we may not be able to complete the development and commercialization of our sulopenem program.

Developing pharmaceutical products is a time-consuming, expensive and uncertain process that takes years to complete. We expect that our expenses will increase substantially as we complete our clinical trials of oral sulopenem and sulopenem, seek marketing approval for such product candidates if clinical trials are successful, and pursue the development of our sulopenem program in additional indications through preclinical and clinical development. If we obtain marketing approval for oral sulopenem, sulopenem

or any future product candidate, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Some of these expenses may be incurred in advance of marketing approval, and could be substantial.

We believe that our existing cash and cash equivalents as of December 31, 2019, together with the net proceeds of approximately $46.7 million that we received in January 2020 from the sale of the Exchangeable Notes and the RLNs (together, the Securities) , will not enable us to fund our operating expenses and capital expenditure requirements for at least the next twelve months from the date of filing this Annual Report on Form 10-K, assuming that our planned programs and expenditures continue and that we do not reduce or eliminate some or all of our research and development programs or commercialization efforts. This condition raises substantial doubt about our ability to continue as a going concern.

We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Although we have successfully raised capital in the past, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to develop and commercialize our sulopenem program and otherwise pursue our business strategy and we may be unable to continue as a going concern.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical product candidates, we are unable to estimate the exact amount of our working capital requirements. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the timing and costs of our ongoing clinical trials of oral sulopenem and sulopenem, including our two ongoing Phase 3 clinical trials;
- the initiation, progress, timing, costs and results of preclinical studies and clinical trials of other potential product candidates and of our current product candidates in additional indications;
- the amount of funding that we receive under government awards that we have applied for or may apply for in the future;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for oral sulopenem and sulopenem and other product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the receipt of marketing approval and revenue received from any potential commercial sales of oral sulopenem and sulopenem;
- the terms and timing of any future collaborations, licensing or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to an exclusive license agreement with Pfizer Inc. (Pfizer) (the Pfizer License) or other future license agreements;
- the amount and timing of any payments we are obligated to make in connection with the RLNs;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;
- the costs of operating as a public company; and
- the extent to which we in-license or acquire other products and technologies.

Provisions in the Private Placement documents may deter or prevent us from raising additional capital to fund our operations.

Provisions in the agreements we entered into in connection with the Private Placement may deter or prevent us from raising additional capital to fund our operations as and when needed. For example, the indenture governing the Exchangeable Notes (the EN Indenture) contains negative covenants prohibiting Iterum Bermuda, as well as us and our wholly owned subsidiaries and their subsidiaries (the Guarantors), who guaranteed Iterum Bermuda's obligations under the Securities, from, among other things, incurring any indebtedness that is not permitted by the EN Indenture and entering into transactions with significant shareholders (as defined in

the EN Indenture). In addition, the indenture governing the RLNs (the RLN Indenture) contains negative covenants prohibiting Iterum Bermuda and the Guarantors from, among other things, selling, transferring or assigning certain assets and taking other actions outside the ordinary course of business that would reasonably be expected to reduce the amount of payments under the RLNs.

In addition, pursuant to the terms of an investor rights agreement we entered into in connection with the Private Placement (the 2020 Investor Rights Agreement), for so long as Sarissa Capital Offshore Master Fund LP, Sarissa Capital Catapult Fund LLC and Sarissa Capital Hawkeye Fund LP (collectively with their affiliates, Sarissa) own 10% of our outstanding ordinary shares on a fully diluted basis, Sarissa has a right of first offer with respect to our future proposed equity financings up to that portion of such new securities which equals Sarissa's then-percentage ownership of our outstanding ordinary shares on a fully diluted basis, subject to specified exceptions for certain exempt issuances and pursuant to specified procedures. These and other provisions in the Private Placement documents could deter or prevent us from raising additional capital. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to develop and commercialize our sulopenem program and otherwise pursue our business strategy and we may be unable to continue as a going concern.

We are substantially dependent on the success of our two product candidates, oral sulopenem and sulopenem, and if we are unable to achieve and sustain profitability, the market value of our ordinary shares will likely decline.

Our ability to become and remain profitable depends on our ability to generate revenue. To date, we have invested substantially all of our efforts and financial resources in the development of oral sulopenem and sulopenem, which are currently our two product candidates in development. Our prospects, including our ability to finance our operations and generate revenue from product sales, will currently depend entirely on the development and commercialization of our sulopenem program.

We do not expect to generate significant revenue unless and until we obtain marketing approval for, and commercialize, oral sulopenem and sulopenem. Our ability to generate future revenue from product sales will require us to be successful in a range of challenging clinical and commercial activities, including:

- enrolling and successfully completing our two ongoing Phase 3 clinical trials and enrolling and successfully completing our planned Phase 1 clinical trials related to pediatric indications;
- applying for and obtaining marketing approval for oral sulopenem and sulopenem;
- protecting and maintaining our rights to our intellectual property portfolio related to our sulopenem program;
- establishing and maintaining supply and manufacturing relationships with third parties that can support clinical development and can provide adequate commercial quantities of oral sulopenem and sulopenem, if approved;
- establishing sales, marketing and distribution capabilities to effectively market and sell oral sulopenem and sulopenem, or entering into collaboration arrangements for the commercialization of oral sulopenem and sulopenem where we choose not to commercialize directly ourselves; and
- obtaining market acceptance of oral sulopenem and sulopenem as viable treatment options.

Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when, or if, we will become profitable. We may never succeed in any or all of these activities and, even if we do, we may never generate revenue that is significant or large enough to achieve profitability. Our expenses could increase if we are required by the FDA, the European Medicines Agency (EMA), or any comparable foreign regulatory authority, to perform different studies or studies in addition to those currently expected, or if there are any delays in completing our clinical trials, including delays or expense associated with increasing the sample size of any study, or with the development of our sulopenem program or any future product candidates. Even if oral sulopenem or sulopenem are approved for commercial sale, we anticipate incurring significant costs associated with the commercial launch of oral sulopenem and sulopenem. Where we enter into collaboration arrangements with third-party collaborators for commercialization of product candidates, our product revenues or the profitability of these product revenues to us would likely be lower than if we were to directly market and sell products in those markets.

Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could cause our shareholders to lose all or part of their investment.

Our indebtedness imposes certain operating and other restrictions on us and could adversely affect our ability to raise additional capital.

On April 27, 2018, our subsidiaries, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited (Borrowers), entered into a loan and security agreement (Loan Agreement) with SVB pursuant to

which SVB agreed to lend the Borrowers up to $30.0 million in two term loans. $15.0 million of the secured credit facility was funded on closing and the other $15.0 million was available at our option upon the satisfaction of certain draw requirements, however, we did not satisfy the second draw conditions before the deadline of October 31, 2019 Obligations under the secured credit facility are secured by substantially all of our existing and future assets and the existing and future assets of our subsidiaries, including intellectual property. Our secured credit facility imposes operating and other restrictions on us. Such restrictions affect, and in many respects limit or prohibit, our ability to, among other things, dispose of certain assets, pay dividends and incur additional indebtedness. Failure to make payments or comply with these and other terms and covenants under our secured credit facility could result in an event of default, which could lead to an acceleration of amounts due and foreclosure upon and/or sale or other liquidation of all of our and our subsidiaries' assets, including intellectual property. Any of the foregoing would have a material adverse effect on our operations and financial condition. In addition, this indebtedness and the security interests granted to secure it could make it more difficult for us to raise additional capital to fund our operations.

In addition, the EN Indenture and the RLN Indenture each contain affirmative and negative covenants which impose operating and other restrictions on us, including, among other things, incurring any indebtedness that is not permitted by the EN Indenture or amending the terms of any subordinated indebtedness, entering into strategic transactions or transferring any material assets and undergoing a change of control transaction (subject to certain exceptions, including in the case of a change of control transaction, a transaction in which each holder of an outstanding Exchangeable Note receives cash consideration of at least 300% of the outstanding principal amount of such Exchangeable Note). Failure to comply with these terms could result in an event of default which could lead, among other things, to an acceleration of amounts due under the EN Indenture and the obligation to pay default interest. Moreover, obtaining a consent to a waiver of these terms is subject to a veto right of the holders of 30% of the outstanding Exchangeable Notes, in the case of the EN Indenture, and 30% of the outstanding RLNs, in the case of the RLN Indenture, and in each case which must include Sarissa so long as Sarissa and its affiliates own at least 10% of the outstanding Exchangeable Notes or RLNs, respectively. This veto right could make it more difficult for us to obtain a waiver than would otherwise be the case. In addition, the rate at which the Exchangeable Notes are exchangeable for our ordinary shares is subject to adjustment, including pursuant to anti-dilution protections. This indebtedness could make it more difficult for us to raise additional capital to fund our operations.

Servicing our indebtedness will require a significant amount of cash, and we may not have sufficient cash flow from our business to pay our indebtedness.

Our ability to make payments of the principal of, to pay interest and special interest on or to refinance our term loan and the Exchangeable Notes, or to make cash payments, if we so elect, in connection with any exchange of Exchangeable Notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow sufficient to service our term loan, the Exchangeable Notes or other indebtedness and make necessary capital expenditures. If we are unable to generate such cash flow , we may be required to adopt one or more alternatives, such as selling assets, restructuring indebtedness or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our term loan, the Exchangeable Notes or other indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

Despite our current debt levels, we may still incur substantially more debt or take other actions that would intensify the risks discussed above.

Despite our current consolidated debt levels, we and our subsidiaries may be able to incur substantial additional debt in the future, subject to the restrictions contained in our current and future debt instruments, some of which may be secured debt. While the Loan Agreement and the EN Indenture restrict our ability to incur additional indebtedness, including secured indebtedness, both allow for certain additional indebtedness and any such restrictions may be waived. In addition, if the Loan Agreement matures or is repaid, we may not be subject to similar restrictions under the terms of any subsequent indebtedness. If new debt is added to our current debt levels, the related risks that we now face could intensify.

We may not have the ability to raise the funds necessary to settle exchanges of the Exchangeable Notes in cash or to repurchase the Exchangeable Notes upon a fundamental change, and the Loan Agreement and our future debt may limit our ability to pay cash upon exchange or repurchase of the Exchangeable Notes.

Holders of the Exchangeable Notes will have the right to require us to repurchase all or a portion of their notes upon the occurrence of a fundamental change at specified repurchase prices. In addition, upon exchange of the Exchangeable Notes, unless we elect to deliver solely ordinary shares to settle such exchange (other than paying cash in lieu of delivering any fractional share), we would be required to make specified cash payments in respect of the Exchangeable Notes being exchanged. However, we may not have enough available cash or be able to obtain financing at the time we are required to make repurchases of Exchangeable Notes

surrendered therefor or to pay cash with respect to Exchangeable Notes being exchanged.In addition, our ability to repurchase or to pay cash upon exchange of the Exchangeable Notes may be limited by law, regulatory authority, the Loan Agreement and future indebtedness.

Our failure to repurchase Exchangeable Notes at a time when the repurchase is required by the EN Indenture or to pay cash upon exchange of the Exchangeable Notes as required by the EN Indenture would constitute a default under the EN Indenture. A default under the EN Indenture or a fundamental change itself could also lead to a default under the Loan Agreement and other agreements governing our future indebtedness. If the payment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the Exchangeable Notes or to pay cash upon exchange of the Exchangeable Notes.

The exchange feature of the Exchangeable Notes may adversely affect our financial condition and operating results.

On or after January 21, 2021 and prior to the earlier of (i) the close of business on the scheduled trading day immediately preceding a mandatory exchange notice for the Exchangeable Notes, which would be triggered by the occurrence of any of certain mandatory exchange trigger events specified in the EN Indenture, and (ii) the close of business on the second scheduled trading day immediately preceding the interest record date, holders of Exchangeable Notes will be entitled to exchange the Exchangeable Notes at any time during at their option. If one or more holders elect to exchange their Exchangeable Notes, unless we elect to satisfy our exchange obligation by delivering solely ordinary shares (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our exchange obligation in cash, which could adversely affect our liquidity. In addition, even if holders do not elect to exchange their Exchangeable Notes, the relevant accounting rules are complex and, depending on how we are required to treat the Exchangeable Notes under applicable accounting rules, our liabilities could be significantly impacted.

We have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We began operations in November 2015. Since our inception, we have devoted substantially all of our financial resources and efforts to organizing and staffing our company, business planning, raising capital, planning for potential commercialization, and research and development, including preclinical and clinical development, for our sulopenem program. While the members of our development team have successfully developed and registered other antibiotics in past roles at different companies, our company has limited experience and has not yet demonstrated an ability to successfully complete a large-scale, pivotal clinical trial, obtain marketing approval, manufacture a commercial scale product (or arrange for a third party to do so on our behalf), or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

Assuming we obtain marketing approval for oral sulopenem and sulopenem, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities whether we choose to commercialize product candidates directly ourselves or seek to commercialize them through third-party collaboration arrangements. We may encounter unforeseen expenses, difficulties, complications and delays, and may not be successful in such a transition.

Raising additional capital may cause dilution to our shareholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Unless and until we can generate a substantial amount of revenue from our sulopenem program or future product candidates, we expect to finance our future cash needs through equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements, marketing and distribution arrangements or government funding. In addition, in connection with the Private Placement, we agreed to undertake an offering of subscription rights to purchase additional Securities (the Rights Offering) to all of our other shareholders. We may also be required to issue ordinary shares upon exchange of the Exchangeable Notes upon the terms and conditions specified therein, which would result in additional dilution to our shareholders. We may also seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. We filed a universal shelf registration statement on Form S-3 (Registration No. 333-232569) with the SEC, which was declared effective on July 16, 2019, and pursuant to which we registered for sale up to $150.0 million of any combination of our ordinary shares, preferred shares, debt securities, warrants and/or units from time to time and at prices and on terms that we may determine.

Our issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our ordinary shares to decline, and our shareholders may not agree with our financing plans or the terms of such financings. To the extent that we raise additional capital through the sale of ordinary shares, convertible securities or other equity securities, the ownership interests of our then existing shareholders may be materially diluted, and the terms of these securities could include

liquidation or other preferences and antidilution protections that could adversely affect the rights of ourthen existing shareholders. Further debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, which could adversely affect our ability to conduct our business. In addition, securing additional financing would require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial resources, we have focused our sulopenem development program on the specific indications of uncomplicated urinary tract infections (uUTI), complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (cIAI), all of which are focused on what we believe to be the most pressing near-term medical needs, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other potential product candidates or developing our sulopenem program in other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

We have broad discretion in the use of our funds and may not use them effectively.

We have broad discretion in the application of our available funds and could spend the funds in ways that do not improve our results of operations or enhance the value of our ordinary shares. Our failure to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our ordinary shares to decline and delay the development of our product candidates. Pending their use, we may invest funds in a manner that does not produce income or that loses value.

Risks Related to Clinical Development and Commercialization

We are heavily dependent on the success of our sulopenem program, and our ability to develop, obtain marketing approval for and successfully commercialize oral sulopenem and sulopenem. If we are unable to obtain marketing approvals for oral sulopenem or sulopenem, or if thereafter we fail to commercialize oral sulopenem or sulopenem or experience significant delays in doing so, our business will be materially harmed.

We currently have no products approved for sale and have invested substantially all of our efforts and financial resources in the development of our sulopenem program as the first and only oral and intravenous (IV) branded penem available globally. Our near-term prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize oral sulopenem and sulopenem. The success of our sulopenem program will depend on several factors, including the following:

- successful enrollment in, and completion of, clinical trials, including completion of our two ongoing Phase 3 clinical trials of oral sulopenem and sulopenem;
- clinical trial results with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- timely completion of any additional clinical trials and non-clinical studies conducted to support the filing for regulatory approvals of our sulopenem program, if required by the FDA or any comparable foreign regulatory authority;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment and maintenance of arrangements with third-party manufacturers to obtain commercial supply at a scale sufficient to meet anticipated demand and at a cost appropriate for our commercialization;

- acquisition and maintenance of patent, trade secret and other intellectual property protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with Pfizer;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of oral sulopenem and sulopenem, if approved, whether alone or in collaboration with others;
- the effectiveness of our own or any future collaborators' marketing, sales and distribution strategy and operations;
- acceptance of oral sulopenem and sulopenem, if approved, by patients, physicians and the medical community at large;
- our ability to obtain and sustain coverage and an adequate level of reimbursement by third-party payors;
- the prevalence, frequency and severity of adverse side effects of oral sulopenem and sulopenem;
- the availability, perceived advantages, relative cost and relative efficacy of alternative and competing therapies; and
- an acceptable safety profile of oral sulopenem and sulopenem following approval.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights, manufacturing and the impact of competition. If we are unable to develop, receive marketing approval for, or successfully commercialize oral sulopenem and sulopenem, or if we experience delays as a result of any of these factors or otherwise, our business could be materially harmed.

Our company has no experience in obtaining regulatory approval for a drug.

Our company has never obtained regulatory approval for, or commercialized, a drug. We must complete extensive preclinical and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals. To gain approval to market a product candidate, we must provide the FDA and foreign regulatory authorities with non-clinical, clinical and chemistry, manufacturing, and controls (CMC) data that adequately demonstrates the safety and efficacy of the product for the intended indication(s) applied for in the new drug application (NDA) or other respective regulatory filing. It is possible that the FDA may refuse to accept any or all of our planned NDAs for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval for any current or future product candidates. If the FDA does not approve any of our planned NDAs, it may require that we conduct additional costly clinical, non-clinical or manufacturing validation studies before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any NDA or other application that we submit may be significantly delayed, possibly for several years, or may require us to expend more resources than we have available.

Any failure or delay in obtaining regulatory approvals would prevent us from commercializing oral sulopenem and sulopenem, generating revenues and achieving and sustaining profitability. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve any NDA or other application that we submit. If any of these outcomes occur, we may be forced to abandon the development of our product candidates, which would materially adversely affect our business and could potentially cause us to cease operations. We face similar risks for our applications in other countries.

If clinical trials of oral sulopenem, sulopenem or any other product candidate that we may advance to clinical trials fail to demonstrate safety and efficacy to the satisfaction of the FDA or comparable foreign regulatory authorities, or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of oral sulopenem, sulopenem or any other product candidate.

We may not commercialize, market, promote, or sell any product candidate in the United States without obtaining marketing approval from the FDA or in other countries without obtaining approvals from comparable foreign regulatory authorities, such as the EMA, and we may never receive such approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We have not previously submitted an NDA to the FDA or similar applications to comparable foreign regulatory authorities for any of our product candidates.

Our business currently depends entirely on the successful development, regulatory approval and commercialization of our sulopenem program. The clinical development of our sulopenem program, or any future product candidates, is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of severe adverse events, failure to comply with protocols or applicable regulatory requirements, and determination by the FDA or any comparable foreign regulatory authority that a drug product is not approvable. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in clinical trials, even after promising results in earlier non-clinical studies or clinical trials. The results of preclinical and other non-clinical studies and/or early clinical trials of our product candidates or future product candidates may not be predictive of the results of later-stage

clinical trials and interim results of a clinical trial do not necessarily predict final results. Notwithstanding any promising results in early non-clinical studies or clinical trials, we cannot be certain that we will not face similar setbacks.

For example, we present data from clinical trials conducted by Pfizer Japan in the 1990s. The data from those clinical trials is not directly comparable to data from clinical trials that would be conducted today or the data that we anticipate from our Phase 3 program for a variety of reasons, including that protocols were designed for different purposes and as a consequence had different enrollment and efficacy evaluation criteria. For example, while a subjective investigator assessment of outcome is typically included in all cUTI protocols and was performed in the Japanese program, more structured endpoints are required as part of current FDA guidelines for registrational trials. Current FDA guidelines define the primary efficacy outcome based on both clinical and microbiological success. The structured endpoint in the Japanese program assessed outcome based on resolution of pyuria and microbiologic outcome. In addition, the pathogens isolated in the course of a clinical trial will vary depending on the types of patients enrolled, the geographic location of the sites that contribute to the study and the year in which the study is performed. While the organisms seen in the Japanese study are similar to those we anticipate in the Phase 3 program, we expect the frequency distribution of these pathogens may be different. Furthermore, adverse event reports can vary by geographic region and we may see a different adverse event rate and different types of events in patients that we study in the Phase 3 program relative to the experience in Japan.

In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Although data from Phase 1 and Phase 2 clinical trials of oral sulopenem and sulopenem provides support for the overall safety profile of the product candidates, many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of our clinical trials warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety and/or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants, among others. It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one of the factors listed or otherwise. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials, we may fail to detect toxicity of or intolerability of our product candidates or may determine that our product candidates are toxic or not well tolerated when that is not in fact the case. In the case of our clinical trials, results may differ on the basis of the type of bacteria with which patients are infected. We cannot assure our shareholders that any ongoing clinical trials that we are conducting or other clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

We may encounter unforeseen events prior to, during, or as a result of, clinical trials that could delay or prevent us from obtaining regulatory approval for oral sulopenem, sulopenem or any of our other product candidates, including:

- although we are conducting our Phase 3 clinical trials pursuant to Special Protocol Assessment (SPA) agreements, the FDA or other comparable foreign regulatory authorities may ultimately disagree as to the design or implementation of our Phase 3 clinical trials or other clinical trials;
- we may not reach agreement on acceptable terms with all clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different trial sites;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the FDA, the local National Health Authorities or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have to suspend or terminate clinical trials of a product candidate for various reasons, including non-compliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we enter into agreement for clinical and commercial supplies; or

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

If we are required to conduct additional clinical trials or other testing of oral sulopenem, sulopenem or any other product candidate beyond the clinical trials and testing that we contemplate, if we are unable to successfully complete clinical trials or other testing of our product candidates, if the results of these clinical trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with oral sulopenem, sulopenem or any other product candidate, we may:

- incur additional unplanned costs;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business. We cannot assure our shareholders that our ongoing Phase 3 clinical trials will be completed on schedule, if at all, or that we will not need to restructure our clinical trials. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of oral sulopenem, sulopenem or any other product candidate.

If we experience delays or difficulties in the enrollment of patients in clinical trials, clinical development activities could be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. While enrollment has completed for all three of our Phase 3 clinical trials, we may not be able to initiate, continue or complete other clinical trials of oral sulopenem, sulopenem or any other product candidate that we develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials as required by the FDA or comparable foreign regulatory authorities, such as the EMA. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for participation in the clinical trial;
- the number of sites at which we conduct the trial and the speed at which we are able to open such sites;
- the prevalence of antibiotic resistance to pathogens where we conduct the clinical trial;
- the accuracy of certain estimates and assumptions upon which the design of the protocols are predicated;
- our ability to recruit clinical trial investigators with appropriate experience;
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications that we are investigating;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before completion.

In addition, we may face competition in enrolling suitable patients as a result of other companies conducting clinical trials for antibiotic product candidates that are intended to treat similar infections, resulting in slower than anticipated enrollment in our clinical trials. Enrollment delays in our clinical trials may result in increased development costs for oral sulopenem and sulopenem, or slow down or halt our product development for oral sulopenem and sulopenem.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, slow down or halt our product candidate development and approval process and jeopardize our ability to seek and obtain the marketing approval required to commence product sales and generate revenue, which would cause the value of our company to decline and limit our ability to obtain additional financing if needed. Furthermore, we rely on and expect to continue to rely on contract research organizations (CROs) and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and we have limited influence over their performance.

Success in non-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot assure our shareholders that any of our ongoing clinical trials or any other clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our sulopenem program in any indication.

Our ongoing Phase 3 clinical trials of oral sulopenem and sulopenem are subject to a number of specific risks arising from our clinical program and the design of such clinical trials.

We have not previously completed Phase 3 clinical trials of oral sulopenem or sulopenem in the indications uUTI and cUTI, and we have not documented to the satisfaction of regulators that these treatments are effective in treating uUTIs and cUTIs in humans. Although we believe that oral sulopenem and sulopenem have the potential to treat uUTIs and cUTIs in humans based on the results of prior preclinical studies and clinical trials, the results of these preclinical studies and clinical trials are not necessarily predictive of the results of our ongoing Phase 3 clinical trials, and we cannot guarantee that oral sulopenem and sulopenem will demonstrate the expected efficacy in clinical trial patients. For example, while we believe that that sulopenem has the potential to treat cIAIs in humans based on the results of prior preclinical studies and clinical trials , sulopenem did not meet the primary FDA endpoint of statistical non-inferiority compared to the control therapy in our Phase 3 cIAI clinical trial. While we believe the secondary supporting analyses and safety data support the potential of sulopenem in the treatment of multi-drug resistant infections, we cannot guarantee that these supporting analyses are indicative of efficacy of sulopenem in treating cIAIs or that they will support any data from our ongoing Phase 3 uUTI and cUTI clinical trials indicating efficacy of oral sulopenem or sulopenem in those indications. We also cannot guarantee that the projections made from the pharmacokinetic and pharmacodynamic models that we developed from non-clinical and clinical oral sulopenem and sulopenem studies will be validated in these clinical trials.

Other companies in the pharmaceutical industry have frequently suffered significant setbacks in later clinical trials, even after achieving promising results in earlier non-clinical studies or clinical trials.

Serious adverse events or undesirable side effects or other unexpected properties of oral sulopenem, sulopenem or any other product candidate may be identified during development or after approval that could delay, prevent or cause the withdrawal of regulatory approval, limit the commercial potential, or result in significant negative consequences following marketing approval.

Serious adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, an institutional review board (IRB), or regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label, the imposition of distribution or use restrictions or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. If oral sulopenem, sulopenem or any of our other product candidates is associated with serious or unexpected adverse events or undesirable side effects, the FDA or the IRBs at the institutions in which our studies are conducted, could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the clinical trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

While the active pharmaceutical ingredient in the bilayer tablet is sulopenem etzadroxil, the combination product with probenecid has not yet been tested extensively in patients. In the cIAI trial, among 668 treated patients, treatment-related adverse events were observed in 6.0% and 5.1% of patients on sulopenem and ertapenem, respectively, with the most commonly reported drug-related adverse event being diarrhea, which was observed in 4.5% and 2.4% of patients on sulopenem and ertapenem, respectively . Discontinuations from treatment were uncommon for both regimens, occurring in 1.5% of patients on sulopenem and 2.1% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 7.5% of patients on sulopenem and 3.6% of patients on ertapenem. While we believe these results support a positive safety and tolerability profile for sulopenem, in future trials there may be unforeseen serious adverse events or side effects that differ from those seen in the cIAI Phase 3 trial, in Phase 1 normal healthy volunteers with oral sulopenem or the prior post-marketing experience with probenecid. There may also be

unexpected adverse events associated with probenecid that have not been seen to date. We may alos see higher rates of adverse events than were reported in the clinical trials Pfizer conducted in Japan.

To date, sulopenem and sulopenem etzadroxil have generally been well tolerated in clinical trials conducted in healthy subjects and patients. During the development of oral sulopenem and sulopenem, patients have experienced drug-related side effects including diarrhea, temporary increases in hepatic enzymes, allergic reactions, and rash. In the Japanese program, one patient reported a serious adverse event related to sulopenem of a transient elevation in liver function tests. The patient died due to metastatic lung cancer. Other serious adverse events recorded in patients receiving sulopenem in the Japanese program, which were not considered by the investigator to be related to sulopenem, included myocardial infarction with respiratory failure and progression of underlying ovarian carcinoma, in both cases resulting in death. For each of these patients, sulopenem was not determined to be the cause of death. If unexpected adverse events occur in any of our clinical trials, we may need to abandon development of our product candidates, or limit development to lower doses or to certain uses or subpopulations in which the undesirable side effects or other unfavorable characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing are later found to cause undesirable or unexpected side effects that prevent further development of the compound.

Undesirable side effects or other unexpected adverse events or properties of oral sulopenem, sulopenem or any of our other product candidates could arise or become known either during clinical development or, if approved, after the approved product has been marketed. If such an event occurs during development, our clinical trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of, or could deny approval of, oral sulopenem, sulopenem or other product candidates. If such an event occurs after such product candidates are approved, a number of potentially significant negative consequences may result, including:

- regulatory authorities may withdraw the approval of such product;
- we may be required to recall a product or change the way such product is administered to patients;
- regulatory authorities may require additional warnings on the label or impose distribution or use restrictions;
- regulatory authorities may require one or more post-marketing studies;
- regulatory authorities may require the addition of a “black box” warning;
- we may be required to implement a Risk Evaluation and Mitigation Strategy (REMS), including the creation of a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- our product may become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate, if approved, or could substantially increase commercialization costs and expenses, which could delay or prevent us from generating revenue from the sale of our products and harm our business and results of operations.

Even if a product candidate does obtain regulatory approval, it may never achieve the market acceptance by physicians, patients, hospitals, third-party payors and others in the medical community that is necessary for commercial success, and the market opportunity may be smaller than we estimate.

Even if we obtain FDA or other regulatory approvals and are able to launch oral sulopenem, sulopenem or any other product candidate commercially, the product candidate may not achieve market acceptance among physicians, patients, hospitals (including pharmacy directors) and third-party payors and, ultimately, may not be commercially successful. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Moreover, many antibiotics currently exist for the pathogens underlying uUTI, cUTI and cIAI. While many of those pathogens are resistant to certain drugs in the market, the selection is broad, and individual physicians’ prescribing patterns vary widely and are affected by resistance rates in their geographies, whether their patients are at elevated risk, the ability of patients to afford branded drugs and concerns regarding generating resistance with specific classes of antibiotics.

Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If oral sulopenem, sulopenem or any other product candidate that we develop does not achieve an adequate level of market acceptance, we may not generate significant product revenues and, therefore, we may not

become profitable. Market acceptance of any product candidate for which we receive approval depends on a number of factors, including:

- the efficacy and safety of the product candidate as demonstrated in clinical trials as compared to alternative treatments;
- the potential and perceived advantages and disadvantages of the product candidates, including cost and clinical benefit relative to alternative treatments;
- relative convenience and ease of administration;
- the clinical indications for which the product candidate is approved;
- the willingness of physicians to prescribe the product;
- the willingness of hospital pharmacy directors to purchase the product for their formularies;
- acceptance by physicians, patients, operators of hospitals and treatment facilities and parties responsible for coverage and reimbursement of the product;
- the availability of coverage and adequate reimbursement by third-party payors and government authorities;
- the effectiveness of our sales and marketing efforts or those of collaborators, where we choose not to commercialize directly ourselves;
- the strength of marketing and distribution support;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling or an approved REMS;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;
- the approval of other new products for the same indications;
- the timing of market introduction of the approved product as well as competitive products;
- adverse publicity about the product or favorable publicity about competitive products;
- the emergence of bacterial resistance to the product; and
- the rate at which resistance to other drugs in the target infections grows.

In addition, the potential market opportunity for oral sulopenem and sulopenem is difficult to estimate. Our estimates of the potential market opportunity are predicated on several key assumptions such as industry knowledge and publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, then the actual market for oral sulopenem and sulopenem could be smaller than our estimates of the potential market opportunity. If the actual market for oral sulopenem and sulopenem is smaller than we expect, or if the product fails to achieve an adequate level of acceptance by physicians, health care payors, patients, hospitals and others in the medical community, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

We currently have no commercial organization. If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing oral sulopenem, sulopenem or any other product candidate if such product candidate is approved.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing oral sulopenem, sulopenem or any other product candidate if such product candidate is approved.

We are currently evaluating our commercialization strategy in the United States and other territories. We are focusing our initial commercial efforts on the United States market, which we believe represents the largest market opportunity for our sulopenem program. We currently do not have a sales, marketing or distribution infrastructure and we have no experience in the sales, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either build our marketing, sales, distribution, managerial and other non-technical capabilities, or make arrangements to outsource those functions to third parties. If oral sulopenem and sulopenem receive regulatory approval, we intend to build a commercial organization and recruit a targeted sales force with technical expertise, an internal marketing and health resource group, as well as a managed markets group

focused on reimbursement activities with third-party payors and a specialty distribution team to ensure pharmacy-level stocking and, where we choose not to commercialize directly ourselves, we will seek to commercialize oral sulopenem and sulopenem through collaboration arrangements. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we intend to target. If we are unable to establish a sales force and marketing and distribution capabilities, our operating results may be adversely affected. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of our product candidates.

Factors that may inhibit our efforts to commercialize our products directly include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- our inability to identify the best territories to target based on resistance statistics and prescribers within those territories;
- the inability of a health resources group to obtain access to educate physicians regarding the attributes of our future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

For those countries in which we choose not to commercialize directly ourselves, which may include the United States, we intend to use collaborators that have direct sales forces and established distribution systems to assist with the commercialization of oral sulopenem, sulopenem and any other product candidate. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us would likely be lower than if we were to directly market and sell products in those markets.

Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we likely would have little control over such third parties, and any of them might fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition from other pharmaceutical and biotechnology companies and our business may suffer if we fail to compete effectively.

The development and commercialization of new drug products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to oral sulopenem, sulopenem and other product candidates that we may seek to develop and commercialize in the future. There are a number of pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of multi-drug resistant infections. Potential competitors also include academic institutions, government agencies and other public and private research organizations. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than oral sulopenem, sulopenem or any other product candidates that we may develop, which could render our product candidates obsolete and noncompetitive.

There are a variety of available oral therapies marketed for the treatment of multi-drug resistant infections that we would expect would compete with oral sulopenem and sulopenem, such as levofloxacin, ciprofloxacin, nitrofurantoin, fosfomycin, amoxicillin-clavulanate, cephalexin and trimethoprim-sulfamethoxazole. Many of the available therapies are well established and widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products, for example in the fluoroquinolone class. If oral sulopenem or sulopenem is approved, the pricing may be at a significant premium over other competitive products that are generic. This may make it difficult for oral sulopenem or sulopenem to compete with these products.

There are also a number of oral product candidates in clinical development by third parties that are intended to treat UTIs. Some mid- to late-stage product candidates include gepotidacin from GlaxoSmithKline, tebipenem pivoxil from Spero Therapeutics, Inc., delafloxacin from Melinta Therapeutics, Inc., pivmecillinam from Utility Therapeutics Limited, and ETX0282CPDP (a novel ß-lactamase inhibitor combined with cefpodoxime proxetil) from Entasis Therapeutics Holdings Inc. If our competitors obtain marketing

approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

There are several IV-administered products marketed for the treatment of infections resistant to first-line therapy for gram-negative infections, including Avycaz from Allergan plc and Pfizer, Vabomere from Melinta Therapeutics, Inc., Zerbaxa from Merck & Co., Zemdri from Cipla, Xerava from Tetraphase Pharmaceuticals, Inc., Recarbrio from Merck & Co, and recently, Fetroja from Shionogi & Co., Ltd. In addition, Nabriva Therapeutics plc's Contepo is an IV-administered product candidate in late-stage clinical development intended to treat resistant gram-negative infections and Allecra Therapeutics recently announced that its IV administered product candidate cefepime-enmetazobactam met the EMA and FDA primary endpoint in its phase 3 clinical trial for the treatment of cUTIs.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, management and sales and marketing personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

In July 2012, the Food and Drug Administration Safety and Innovation Act was passed, which included the Generating Antibiotics Incentives Now Act (the GAIN Act). The GAIN Act is intended to provide incentives for the development of new, qualified infectious disease products (QIDP). One such incentive is that, once a product receives QIDP designation and completes the necessary clinical trials and is approved by the FDA, it will be given an additional five years of regulatory exclusivity regardless of whether it is protected by a patent, provided that it is already eligible for another type of regulatory exclusivity. The FDA has designated sulopenem and oral sulopenem as QIDPs for the indications of uUTI, cUTI, cIAI, community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. In December 2016, the Cures Act was passed, providing additional support for the development of new infectious disease products. These incentives may result in more competition in the market for new antibiotics, and may cause pharmaceutical and biotechnology companies with more resources than we have to shift their efforts towards the development of product candidates that could be competitive with oral sulopenem, sulopenem and our other product candidates.

Even if we are able to commercialize oral sulopenem, sulopenem or any other product candidate, the product may become subject to unfavorable pricing regulations, or third-party payor coverage and reimbursement policies that could harm our business.

Marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, which may negatively affect the revenues that we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

The commercial success of oral sulopenem and any future product candidates, if approved, will depend substantially, both in the United States and outside the United States, on the extent to which coverage and adequate reimbursement for the product and related treatments are available from government health programs, private health insurers and other third-party payors. If coverage is not available, or reimbursement is limited, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investments. Government authorities and third-party payors, such as health insurers and managed care organizations, publish formularies that identify the medications they will cover and the related payment levels. The healthcare industry is focused on cost containment, both in the United States and elsewhere. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell our product candidates profitably.

In the United States, sales of our product candidates will depend, in part, on the availability and extent of coverage and reimbursement by third-party payors, such as government health programs, including Medicare and Medicaid, commercial insurance and managed healthcare organizations. There is no uniform coverage and reimbursement policy among third-party payors; however, private third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Obtaining coverage and reimbursement approval for a product candidate from third-party payors is a time-consuming and costly

process that may require the provision of supporting scientific, clinical and cost effectiveness data for the use ofsuch product candidate to the third-party payor. There may be significant delays in obtaining such coverage and reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product candidate is approved by the FDA. Moreover, eligibility for coverage and reimbursement does not imply that a product candidate will be paid for in all cases or at a rate that covers operating costs, including research, development, intellectual property, manufacture, sales and distribution expenses. Reimbursement rates may vary according to the use of the product candidate and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. It is difficult to predict what third-party payors will decide with respect to coverage and reimbursement for our product candidates.

We currently expect that sulopenem IV, if approved, will be administered in a hospital setting, and oral sulopenem, if approved, will be used in a community setting and possibly be administered in a hospital inpatient setting as well. In the United States, third-party payors generally reimburse hospitals a single bundled payment established on a prospective basis intended to cover all items and services provided to the patient during a single hospitalization. Hospitals bill third-party payors for all or a portion of the fees associated with the patient's hospitalization and bill patients for any deductibles or co-payments. Because there is typically no separate reimbursement for drugs administered in a hospital inpatient setting, some of our target customers may be unwilling to adopt our product candidates in light of the additional associated cost. If we are forced to lower the price we charge for our product candidates, if approved, our gross margins may decrease, which would adversely affect our ability to invest in and grow our business. Centers for Medicare and Medicaid Services (CMS) recently revised its reimbursement system for certain antibiotics in order to address challenges associated with antimicrobial resistance. Based on the final rule published on August 2, 2019, CMS is finalizing an alternative new technology add-on payment pathway for certain breakthrough devices, and under this policy, a QIDP product will be considered new and will not need to demonstrate that it meets the substantial clinical improvement criterion. Instead it will only need to meet the cost criterion. CMS has also increased the new technology add-on payment percentage to 75 percent for an antimicrobial designated by the FDA as a QIDP. As this rule has only recently been implemented, we cannot at present assess its potential impact on sulopenem.

An inability to promptly obtain coverage and adequate payment rates from third-party payors for any approved product candidates that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

We cannot predict whether bacteria may develop resistance to oral sulopenem or sulopenem, which could affect their revenue potential.

We are developing oral sulopenem and sulopenem to treat drug-resistant bacterial infections. The bacteria responsible for these infections evolve quickly and readily transfer their resistance mechanisms within and between species. We cannot predict whether or when bacterial resistance to oral sulopenem and sulopenem may develop.

As with some commercially available carbapenems, oral sulopenem and sulopenem are not active against organisms expressing a resistance mechanism mediated by enzymes known as carbapenemases. Although occurrence of this resistance mechanism is currently uncommon, we cannot predict whether carbapenemase-mediated resistance will become widespread in regions where we intend to market sulopenem if it is approved. The use of carbapenems or penems in areas with drug-resistant infections or in countries with poor public health infrastructures, or the potentially extensive use of oral sulopenem or sulopenem outside of controlled hospital settings or in the community, could contribute to the rise of resistance. In addition, prescribers may be less likely to prescribe oral sulopenem and sulopenem if they are concerned about contributing to the rise of antibiotic resistance. If resistance to oral sulopenem or sulopenem becomes prevalent, or concerns about such resistance are strong, our ability to generate revenue from oral sulopenem and sulopenem could suffer.

We may be subject to costly product liability claims related to our clinical trials and product candidates and, if we are unable to obtain adequate insurance or are required to pay for liabilities resulting from a claim excluded from, or beyond the limits of our insurance coverage, a material liability claim could adversely affect our financial condition.

Because we conduct clinical trials with human patients, we face the risk that the use of our product candidates may result in adverse side effects to patients in our clinical trials. We face even greater risks upon any commercialization of our product candidates. Although we have product liability insurance, which covers our clinical trials for up to $10.0 million, our insurance may be insufficient to reimburse us for any expenses or losses we may suffer. We will need to increase our insurance coverage if and when we receive marketing approval for and begin selling oral sulopenem, sulopenem or any other product candidate. We do not know whether we will be able to continue to obtain product liability coverage and obtain expanded coverage if we require it, on acceptable terms, if at all.

We may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage. Where we have provided indemnities in favor of third parties under our agreements with them, there is also a risk

that these third parties could incur a liability and bring a claim under such indemnities. An individual may bring a product liability claim against us alleging that one of our product candidates or products causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

- withdrawal of clinical trial volunteers, investigators, patients or trial sites;
- the inability to commercialize our product candidates;
- decreased demand for our product candidates;
- regulatory investigations that could require costly recalls or product modifications;
- loss of revenue;
- substantial costs of litigation;
- liabilities that substantially exceed our product liability insurance, which we would then be required to pay ourselves;
- an increase in our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, if at all;
- the diversion of management's attention from our business; and
- damage to our reputation and the reputation of our products.

Our operations, including our use of hazardous materials, chemicals, bacteria and viruses, require us to comply with regulatory requirements and expose us to significant potential liabilities.

Our operations involve the use of hazardous materials, including chemicals, and may produce dangerous waste products. Accordingly, we, along with the third parties that conduct clinical trials and manufacture our products and product candidates on our behalf, are subject to federal, state, local and foreign laws and regulations that govern the use, manufacture, distribution, storage, handling, exposure, disposal and recordkeeping with respect to these materials. We are also subject to a variety of environmental and occupational health and safety laws. Compliance with current or future laws and regulations can require significant costs and we could be subject to substantial fines and penalties in the event of non-compliance. In addition, the risk of contamination or injury from these materials cannot be completely eliminated. In such event, we could be held liable for substantial civil damages or costs associated with the cleanup of hazardous materials.

If we experience a significant disruption in our information technology systems or breaches of data security, our business could be adversely affected.

We rely on information technology systems to keep financial records, capture laboratory data, maintain clinical trial data and corporate records, communicate with staff and external parties and operate other critical functions. Our information technology systems are potentially vulnerable to disruption due to breakdown, malicious intrusion and computer viruses or other disruptive events including, but not limited to, natural disaster. If we were to experience a prolonged system disruption in our information technology systems or those of certain of our vendors, it could delay or negatively impact the development and commercialization of our sulopenem program and any future product candidates or technology, which could adversely impact our business. Although we maintain offsite back-ups of our data, if operations at our facilities were disrupted, it may cause a material disruption in our business if we are not capable of restoring function on an acceptable timeframe. In addition, our information technology systems are potentially vulnerable to data security breaches—whether by employees or others—which may expose sensitive data to unauthorized persons. Such data security breaches could lead to the loss of trade secrets or other intellectual property or, could lead to the public exposure of personal information (including sensitive personal information) of our employees and others, any of which could have a material adverse effect on our business, financial condition and results of operations. Moreover, a security breach or privacy violation that leads to disclosure or modification of, personally identifiable information, could harm our reputation, compel us to comply with applicable European, and United States federal and/or state, breach notification laws, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to litigation and liability under laws and regulations that protect personal data, resulting in increased costs or loss of revenue. In addition, a data security breach could result in loss of clinical trial data or damage to the integrity of that data. If we are unable to prevent such security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer reputational damage, financial loss and other negative consequences because of lost or misappropriated information. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above.

Risks Related to Our Dependence on Third Parties

If we fail to comply with our obligations in our agreement with Pfizer, we could lose such rights that are important to our business.

We rely heavily on the Pfizer License pursuant to which we exclusively in-license certain patent rights and know-how related to sulopenem etzadroxil and certain know-how related to the IV formulation of sulopenem. The Pfizer License imposes diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us, and we may enter into additional agreements, including license agreements, with other parties in the future which impose similar obligations.

The Pfizer License gives us exclusive worldwide rights to develop, manufacture, and commercialize sulopenem etzadroxil and sulopenem, or any other prodrug of sulopenem previously identified by Pfizer as well as the right to use relevant information and regulatory documentation developed by Pfizer to support any regulatory filing worldwide. In exchange for those rights, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop, obtain regulatory approval for and commercialize sulopenem etzadroxil and sulopenem by implementing a specified development plan and providing an update on progress on an annual basis. Under the Pfizer License, we paid Pfizer a one-time non-refundable upfront fee of $5.0 million, clinical milestone payments totaling $15.0 million, upon first patient dosing of oral sulopenem and sulopenem in a Phase 3 clinical trial, and are obligated to pay Pfizer milestone payments upon the achievement of other specified regulatory and sales milestones as well as royalties ranging from a single-digit to mid-teens percentage based on the amount of marginal net sales of each licensed product. Pfizer also received 381,922 of our Series A preferred shares (which converted to ordinary shares in connection with our IPO) as additional payment for the licensed rights.

If we fail to comply with our obligations to Pfizer under the Pfizer License, Pfizer may have the right to terminate the Pfizer License, in which event we would not be able to develop, obtain regulatory approval for, manufacture or market any product candidate that is covered by the Pfizer License, including sulopenem etzadroxil and sulopenem, which would materially harm our business, financial condition, results of operations and growth prospects. Any termination of the Pfizer License or reduction or elimination of our rights thereunder may result in our having to negotiate new or reinstated agreements with less favorable terms. Any termination of the Pfizer License would cause us to lose our rights to important intellectual property or technology.

We expect to depend on collaborations with third parties for the development and commercialization of oral sulopenem and sulopenem in certain territories. Our prospects with respect to those product candidates will depend in part on the success of those collaborations.

Although we are focusing our initial commercial efforts on the United States market, which we believe represents the largest market opportunity for our sulopenem program, we are also evaluating our commercialization strategy both within and outside the United States. For those countries in which we choose not to commercialize directly ourselves, we intend to seek to commercialize oral sulopenem and sulopenem through collaboration arrangements. In addition, we may seek third-party collaborators for development and commercialization of other product candidates in the United States and other territories. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangements but plan to initiate discussions with potential commercial partners. The EN Indenture and RLN Indenture each contain restrictions on entering into collaborations requiring consent of a portion of the holders of each of the Exchangeable Notes and RLNs. There is no guarantee that consent will be forthcoming.

We may derive revenue from research and development fees, license fees, milestone payments and royalties under any collaborative arrangement into which we enter. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, our collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms. As a result, we can expect to relinquish some or all of the control over the future success of a product candidate that we license to a third party.

We face significant competition in seeking and obtaining appropriate collaborators. Collaborations involving our product candidates may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time consuming and expensive;
- collaborators may not properly maintain, defend or enforce our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

We rely on third parties to conduct our preclinical studies and our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize any of our product candidates. If they do not perform satisfactorily, our business may be materially harmed.

We do not independently conduct non-clinical studies that comply with good laboratory practice (GLP) requirements. We also do not have the ability to independently conduct clinical trials of any of our product candidates. We rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators to conduct our clinical trials of oral sulopenem and sulopenem and expect to rely on these third parties to conduct clinical trials of any potential product candidates. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for clinical development activities limits our control over these activities but we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a CRO for a clinical trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the clinical trial. While we will have agreements governing their activities, we control only certain aspects of their activities and have limited influence over their actual performance. The third parties with whom we contract for execution of our GLP studies and our clinical trials play a significant role in the conduct of these studies and clinical trials and the subsequent collection and analysis of data. Although we rely on these third parties to conduct our GLP-compliant non-clinical studies and clinical trials, we remain responsible for ensuring that each of our non-clinical studies and clinical trials are conducted in accordance with applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. The FDA and regulatory authorities in other jurisdictions also require us to comply with standards, commonly referred to as good clinical practices (GCPs), for conducting, monitoring, recording and reporting the results of clinical trials to assure that data and reported results are accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot assure our shareholders that, upon inspection, the FDA will determine that any of our clinical trials comply with GCPs. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates. If that occurs, we may not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for oral sulopenem, sulopenem or other product candidates could be harmed, our costs could increase and our ability to generate revenue could be delayed, impaired or foreclosed.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of preclinical and clinical supplies of oral sulopenem and sulopenem and expect to continue to do so in connection with any future commercialization and for any future clinical trials and commercialization of our product candidates and potential product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have the internal infrastructure or capability to manufacture oral sulopenem and sulopenem for use in the conduct of our preclinical research or clinical trials. We rely on third-party contract manufacturers to manufacture supplies of oral sulopenem and sulopenem, and we expect to rely on third-party contract manufacturers to manufacture commercial quantities of any product candidate that we commercialize following approval for marketing by applicable regulatory authorities, if any. Reliance on third-party manufacturers entails risks, including:

- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of their agreement with us;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- the possible breach of the manufacturing agreement by the third party;
- the failure of the third-party manufacturer to comply with applicable regulatory requirements; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

We currently rely on a small number of third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our preclinical research and clinical trials. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates although negotiations are well advanced. If any of our existing manufacturers should become unavailable to us for any reason, we may incur delays in identifying or qualifying replacements.

We will enter into agreements with third-party contract manufacturers for the commercial production of oral sulopenem and sulopenem. This process is difficult and time consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under current Good Manufacturing Practices, or cGMPs, that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be approved by the FDA after we submit an NDA and before potential approval of the product candidate. Similar regulations apply to manufacturers of our product candidates for use or sale in countries outside of the United States. We have no direct control over the ability of our third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel, and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our product candidates. If our manufacturers cannot successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate. In addition, our manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us,

including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and have a material adverse effect on our business, financial condition and results of operations.

We and our third-party suppliers also continue to refine and improve the manufacturing process, certain aspects of which are complex and unique, and we may encounter difficulties with new or existing processes, particularly as we seek to significantly increase our capacity to commercialize oral sulopenem and sulopenem. Our reliance on contract manufacturers also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

As drug candidates are developed through non-clinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, methods of making drug formulations, and drug formulations, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our drug candidates to perform differently and affect the results of clinical trials or other future clinical trials conducted with the altered materials. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our drug candidates and jeopardize our ability to commence sales and generate revenue.

Our current and anticipated future dependence upon others for the manufacture of oral sulopenem and sulopenem and any future product candidates may adversely affect our future profit margins and our ability to commercialize any products for which we receive marketing approval on a timely and competitive basis.

Risks Related to Our Intellectual Property

We rely heavily on the Pfizer License for the patent rights and know-how required to develop and commercialize oral sulopenem and the know-how required to develop the IV formulation of sulopenem.

We currently do not own any patents and rely heavily on the Pfizer License for intellectual property rights that are important or necessary for the development of oral sulopenem and sulopenem. We do not own or license any patent rights that cover the IV formulation of sulopenem. In addition, all patents directed to the compound sulopenem expired prior to us entering into the Pfizer License. Licenses to additional third-party intellectual property, technology and materials that may be required for the development and commercialization of our sulopenem program or any other product candidates or technology may not be available at all or on commercially reasonable terms. In that event, we may be required to expend significant time and resources to redesign our sulopenem program and any other product candidates or technology we may obtain in the future or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize oral sulopenem or sulopenem or other future product candidates or technologies, which could materially harm our business, financial condition, results of operations and growth prospects.

Under the Pfizer License, and we expect under certain of our future license agreements, we are responsible for prosecution and maintenance of the licensed patents and for bringing any actions against any third party for infringing on such patents. In addition, the Pfizer License requires, and we expect certain of our future license agreements would also require, us to meet certain development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. In addition, such license agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Disputes may arise regarding intellectual property subject to the Pfizer License or any of our future license agreements, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe, misappropriate or otherwise violate any intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under the license agreement;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In spite of our best efforts, Pfizer and any potential future licensors might conclude that we have materially breached our license agreements and might therefore terminate the relevant license agreements, thereby removing our ability to develop and commercialize products and technology covered by such license agreements. If any of our inbound license agreements are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and growth prospects.

If we are unable to obtain and maintain patent protection or other intellectual property rights for oral sulopenem or our other technology and product candidates, or if the scope of the patent protection or intellectual property rights we obtain is not sufficiently broad, we may not be able to successfully develop or commercialize oral sulopenem or any other product candidates or technology or otherwise compete effectively in our markets.

We rely upon a combination of patents, trademarks, trade secret protection, confidentiality agreements and other proprietary rights to protect the intellectual property related to our development programs and product candidates. Our success depends, in part, on obtaining and maintaining patent protection and successfully enforcing these patents and defending them against third-party challenges in the United States and other countries. If we or our licensors are unable to obtain or maintain patent protection with respect to oral sulopenem or any other product candidates or technology we develop, our business, financial condition, results of operations and growth prospects could be materially harmed.

We have sought to protect our proprietary position by in-licensing patents in the United States and abroad related to oral sulopenem. The patent prosecution process is expensive and time-consuming, and we and our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, although we control prosecution of the patents we have licensed from Pfizer related to our sulopenem program, we may not always have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce or defend the patents, covering technology that we may license from third parties. Therefore, these patents and patent applications may not be prosecuted, maintained, enforced or defended in a manner consistent with the best interests of our business.

If any patent applications we may own or in-license in the future with respect to our development programs or product candidates fail to issue, if their breadth or strength of protection is threatened or if they fail to provide meaningful exclusivity for our current and future product candidates, it could dissuade companies from collaborating with us to develop product candidates and threaten our ability to commercialize products. Any such outcome could materially harm our competitive position, business, financial condition, results of operations and growth prospects.

The patent position of pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of countries outside the United States may not protect our rights to the same extent as the laws of the United States. For example, EU patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. In addition, publications of discoveries in scientific literature often lag behind the actual discoveries, patent applications in the United States and other jurisdictions remain confidential for a period after filing, and some remain so until issued. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in the patents or pending patent applications we currently own, license or may own or license in the future, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. There is no assurance that all potentially relevant prior art relating to our patent rights has been found, and such prior art could potentially invalidate one or more of the patents we currently license or may own or license in the future or prevent a patent from issuing from one or more pending patent applications we own or may own or license in the future. There is also no assurance that prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patent rights, may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. Even if patents do successfully issue and even if such patents cover our current and future product candidates, third parties may challenge their ownership, validity, enforceability or scope, which may result in such patents being narrowed, invalidated or held unenforceable, which could allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Any successful opposition to these patents or any other patents owned by us in the future or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Furthermore, even if they are unchallenged, our patents rights may not adequately protect our product candidates and technology, provide exclusivity for our product candidates, prevent others from designing around our claims or provide us with a competitive advantage. Any of these outcomes could impair our ability to prevent competition from third parties. Changes in either the patent laws or interpretation of the patent laws in the United States or other countries may diminish the value of our patent rights or narrow the scope of our patent protection.

We cannot offer any assurances about whether any issued patents will be found invalid and unenforceable or will be challenged by third parties. Any successful challenge or opposition to patents owned by or licensed to us could deprive us of rights necessary for

the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

Furthermore, our patent rights may be subject to a reservation of rights by one or more third parties. For example, certain research we conducted was funded in part by the U.S. government. As a result, the U.S. government may have certain march-in rights to patents and technology arising out of such research, if any. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations and growth prospects.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third party patent which might adversely affect our ability to develop and market our product candidates.

We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, U.S. applications filed before November 29, 2000 and certain U.S. applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

The patent protection for our product candidates may expire before we are able to maximize their commercial value which may subject us to increased competition and reduce or eliminate our opportunity to generate product revenue.

Patents have a limited lifespan. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. The patents for our product candidates have varying expiration dates and, if these patents expire, we may be subject to increased competition and we may not be able to recover our development costs. For example, our licensed U.S. patent claim for a composition of matter patent for oral sulopenem is due to expire in 2029, subject to potential extension to 2034 under the Drug Price Competition and Patent Term Restoration Act of 1984 (referred to as the Hatch-Waxman Act). Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our patent rights may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

The FDA designated sulopenem and oral sulopenem as QIDPs for the indications of uUTI, cUTI, cIAI, community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. QIDP status provides the potential for a more rapid review cycle for an NDA and could add five years to any regulatory exclusivity period that we may be granted. However, that does not guarantee that we will receive any regulatory exclusivity or that any such exclusivity will be for a period sufficient to provide us with any commercial advantage. Moreover, we do not own or license any patent directed to the compound sulopenem.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of the U.S. patents we currently license may be eligible for limited patent term extension under the Hatch-Waxman Act, and similar legislation in the European Union. The Hatch-Waxman Act permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process.

A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. We may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of the relevant patents or otherwise fail to satisfy applicable requirements and the length of the extension could be less than we request. To the extent we wish to pursue patent term extension based on a patent that we in-license from Pfizer or another third party, we would need the cooperation of Pfizer or the third party. Moreover, similar extensions may be available in some of the larger economic territories but may not be available in all of our markets of interest.

If we are unable to obtain patent term extension/restoration or some other exclusivity, or the term of any such extension is less than we request, the period during which we can enforce our exclusive rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, we could be subject to increased competition and our opportunity to establish or maintain product revenue could be substantially reduced or eliminated. Furthermore, we may not have sufficient time to recover our development costs prior to the expiration of our U.S. and non-U.S. patent rights. If this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. Any of the foregoing would materially harm our business, financial condition, results of operations and growth prospects.

Intellectual property rights do not necessarily address all potential threats to our business.

Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, *inter partes* review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether. In addition, the degree of future protection afforded by our intellectual property rights is uncertain because even granted intellectual property rights have limitations, and may not adequately protect our business. The following examples are illustrative:

- others may be able to make compounds or formulations that are similar to oral sulopenem and sulopenem compounds or formulations but that are not covered by the claims of our patent rights;
- the patents of third parties may have an adverse effect on our business;
- we or our licensors or any future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by the issued patents that we own or have exclusively licensed;
- we or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible our pending patent applications, and any future patent applications, will not lead to issued patents or afford meaningful protection for our product candidates;
- issued patents that we may own in the future or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- third parties performing manufacturing or testing for us using our product candidates or technologies could use the intellectual property of others without obtaining a proper license; and
- we may not develop additional proprietary technologies that are patentable.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the pharmaceutical industry involves both technological complexity and legal complexity.

Therefore, obtaining and enforcing pharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the America Invents Act (the AIA) was signed into law on September 16, 2011, and many of its substantive changes became effective on March 16, 2013.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the U.S. Patent and Trademark Office, or USPTO, after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO, including through post-issuance patent review procedures such as *inter partes* review, post-grant review and covered business methods. This applies to all U.S. patents, including those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

In the last few years, the USPTO has developed regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA, in particular, the first to file provisions only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the AIA will have on the operation of our business and this may not be known until such time as we, or our licensors or collaboration partners, are filing patent applications for an invention or seeking to defend issued patents. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' or collaboration partners' patent applications and the enforcement or defense of our or our licensors' or collaboration partners' issued patents, all of which could have an adverse effect on our business and financial condition.

Moreover, the standards that the USPTO and foreign patent office's use to grant patents are not always applied predictably or uniformly and can change. Consequently, any patents we currently license or may own or license in the future may have a shorter patent term than expected or may not contain claims that will permit us to stop competitors from using our technology or similar technology or from copying our products. Similarly, the standards that courts use to interpret patents are not always applied predictably or uniformly and may evolve, particularly as new technologies develop. In addition, changes to patent laws in the United States or other countries may be applied retroactively to affect the ownership, validity, enforceability or term of patents we currently license or may own or license in the future.

For example, the U.S. Supreme Court's rulings on several patent cases in recent years, such as*Association for Molecular Pathology v. Myriad Genetics, Inc*., *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, and *Alice Corporation Pty. Ltd. v. CLS Bank International*, either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Similarly, the complexity and uncertainty of European patent laws has also increased in recent years. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution. These changes could limit our ability to obtain new patents in the future that may be important for our business.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe, misappropriate or otherwise violate our patents, trademarks, copyrights or other intellectual property or those of our licensors. To counter infringement, misappropriation, unauthorized use or other violations, we may be required to file legal claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. We may not be able to prevent, alone or with our licensors, infringement, misappropriation or other violations of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is

also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement, misappropriation or other intellectual property litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business.

Our commercial success depends, in part, upon our ability, and the ability of our future collaborators, to develop, manufacture, market and sell oral sulopenem, sulopenem and any future product candidates, if approved, and use our proprietary technologies without alleged or actual infringement, misappropriation or other violation of the patents and other intellectual property rights of third parties. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties.

We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to oral sulopenem, sulopenem or any future product candidates and technology, including interference or derivation proceedings, post grant review and *inter partes* review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Similarly, we or our licensors or collaborators may initiate such proceedings or litigation against third parties, e.g., to challenge the validity or scope of intellectual property rights controlled by third parties. In order to successfully challenge the validity of any U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court would invalidate the claims of any such U.S. patent. Moreover, third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be nonexclusive, thereby giving our competitors access to the same technologies licensed to us. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In such an event, we would be unable to further practice our technologies or develop and commercialize any of our product candidates at issue, which could harm our business significantly.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates, if approved. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee time and resources from our business. Third parties making such claims may have the ability to dedicate substantially greater resources to these

legal actions than we or our licensors or collaborators can. In the event of a successful claim of infringement, misappropriation or other violation against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. In addition to infringement claims against us, we may become a party to other patent litigation and other adversarial proceedings such as proceedings before the Patent Trial and Appeal Board and opposition proceedings in the European Patent Office regarding intellectual property rights with respect to our products and technology.

Patent litigation and other proceedings may also absorb significant management time. The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. During the course of any patent or other intellectual property litigation or other proceeding, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings or developments and if securities analysts or investors regard these announcements as negative, the perceived value of our product candidates or intellectual property could be diminished. Accordingly, the market price of our ordinary shares may decline. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our business, ability to compete in the marketplace, financial condition, results of operations and growth prospects.

We may not be able to protect our intellectual property rights globally, which could negatively impact our business.

Filing, prosecuting and defending patents covering oral sulopenem, sulopenem and any future product candidates globally would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Further, licensing partners may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and any current or future patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets.

Additionally, the requirements for patentability may differ in certain countries, particularly developing countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval of a drug and its patent status. Furthermore, generic or biosimilar drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic or biosimilar drug manufacturers may develop, seek approval for, and launch biosimilar versions of our products. In addition, certain countries in Europe and developing countries, including China and India, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our and our licensors' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

We may be subject to claims that we or our employees, consultants, contractors or advisors have infringed, misappropriated or otherwise violated the intellectual property of a third party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the intellectual property and other proprietary information, know-how or trade secrets of others in their work for us, we may be subject to claims that we or these employees have used or disclosed such intellectual property or other proprietary information. Litigation may be necessary to defend against these claims.

In addition, we may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. While we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. To the extent that we fail to obtain such assignments, such assignments do not contain a self-executing assignment of intellectual property rights or such assignments are breached, we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or a patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents covering our products, our competitors might be able to enter the market, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, in seeking to develop and maintain a competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, independent contractors, advisors, corporate collaborators, outside scientific collaborators, contract manufacturers, suppliers and other third parties. We, as well as our licensors, also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time consuming and the outcome is unpredictable. In addition, some courts both within and outside the United States may be less willing or unwilling to protect trade secrets. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

Trade secrets and know-how can be difficult to protect as trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. If we fail to prevent material disclosure of the know-how, trade secrets and other intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition. Even if we are able to adequately protect our trade secrets and proprietary information, our trade secrets could otherwise become known or could be independently discovered by our competitors. For example, competitors could purchase our products and attempt to replicate some or all of the competitive advantages we derive from our development efforts, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, in the absence of patent protection, we would have no right to prevent them, or those to whom they communicate, from using that technology or information to compete with us.

We may not be able to prevent misappropriation of our intellectual property, trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

We have not yet registered our trademarks in certain jurisdictions. Failure to secure those registrations could adversely affect our business.

We have registered trademarks for "Iterum" in the United States, European Union, Japan, Switzerland and Canada. If we are unable to secure registrations for our trademarks in other countries, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could adversely affect our business. We are in the process of registering trademarks for our product candidates in the United States, Europe and Canada. Any trademark applications we have filed for our product candidates or may file in the future are not guaranteed to be allowed for registration, and even if they are, we may fail to maintain or enforce such registered trademarks. During trademark registration proceedings in the United States, Europe, Canada and other jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the USPTO and in comparable agencies in many other jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

In addition, any proprietary name we propose to use with oral sulopenem, sulopenem or any other product candidate in the United States must be approved by the FDA, and in Europe by the EMA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA and the EMA each typically conduct a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA or the EMA object to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe, misappropriate or otherwise violate the existing rights of third parties and be acceptable to the FDA and the EMA.

Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our business, financial condition, results of operations and growth prospects.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize oral sulopenem, sulopenem or other future product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates, oral sulopenem and sulopenem, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities, with regulations differing from country to country. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We currently do not have any products approved for sale in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process.

Although we have QIDP status and fast track designation for sulopenem and oral sulopenem for the indications of uUTI, cUTI and cIAI (and for the indications of community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and

pelvic inflammatory disease) which may provide for a more rapid new drug application review cycle, the time required to obtain approval, if any, by the FDA and comparable foreign authorities is unpredictable and typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States until we or they receive regulatory approval of an NDA from the FDA.

In order to obtain approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from non-clinical studies and clinical trials can be interpreted in different ways. Even if we believe that the non-clinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Although we are conducting our Phase 3 clinical trials pursuant to SPA agreements, the FDA may still require us to conduct additional non-clinical studies or clinical trials for our product candidates either prior to or post-approval, and it may otherwise object to elements of our clinical development program.

We have not submitted an NDA for any of our product candidates. An NDA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and efficacy for each desired indication. The NDA must also include significant information regarding the chemistry, manufacturing and controls for the product candidate. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. The FDA has substantial discretion in the review and approval process and may refuse to accept for filing any application or may decide that our data is insufficient for approval and require additional non-clinical, clinical or other studies. Foreign regulatory authorities have differing requirements for approval of drugs with which we must comply prior to marketing. Obtaining marketing approval for marketing of a product candidate in one country does not ensure that we will be able to obtain marketing approval in other countries, but the failure to obtain marketing approval in one jurisdiction could negatively affect our ability to obtain marketing approval in other jurisdictions. The FDA or any foreign regulatory body can delay, limit or deny approval of our product candidates or require us to conduct additional non-clinical or clinical testing or abandon a program for many reasons, including:

- the FDA or the applicable foreign regulatory agency's disagreement with the design or implementation of our clinical trials, although we are conducting our Phase 3 clinical trials pursuant to SPA agreements;
- negative or ambiguous results from our clinical trials or results that may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory body that our product candidates are safe and effective for the proposed indication(s);
- the FDA's or the applicable foreign regulatory agency's disagreement with the interpretation of data from non-clinical studies or clinical trials;
- our inability to demonstrate the clinical and other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's or the applicable foreign regulatory agency's requirement for additional non-clinical studies or clinical trials;
- the FDA's or the applicable foreign regulatory agency's disagreement regarding the formulation, labeling and/or the specifications for our product candidates; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage complete the FDA or foreign regulatory approval processes and are successfully commercialized. The lengthy review process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval, which would significantly harm our business, financial condition, results of operations and growth prospects.

Even if we eventually receive approval of an NDA or foreign marketing application for our product candidates, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, often referred to as Phase 4 clinical trials, and the FDA may require the implementation of a REMS, which may be required to ensure safe

use of the drug after approval. The FDA or the applicable regulatory agency also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

Future legislation and/or regulations and policies adopted by the FDA, the EMA or similar regulatory authorities may increase the time and cost required for us to conduct and complete clinical trials of oral sulopenem, sulopenem and other potential product candidates.

The FDA has established regulations to govern the drug development and approval process, as have foreign regulatory authorities. The policies of the FDA and other regulatory authorities may change and additional laws may be enacted or government regulations may be promulgated that could prevent, limit, delay, or alternatively accelerate regulatory review of our product candidates.

If we are unable to obtain marketing approval in jurisdictions outside the United States, we will not be able to market our product candidates outside of the United States.

In order to market and sell oral sulopenem, sulopenem or our other future product candidates in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis or at all.

We are currently evaluating our commercialization strategy in the United States and other territories. We believe that in addition to the United States, Europe represents a significant market opportunity because of rising rates of extended spectrum ß-lactamases (ESBL) resistance.

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the United Kingdom will not accept high regulatory alignment with the European Union.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

Non-U.S. regulatory authorities may require us to conduct additional clinical trials or non-clinical studies to accommodate submission for the cUTI indication.

We obtained scientific advice from the EMA for each of the Phase 3 clinical trials in the uUTI, cUTI and cIAI indications, as well as to gain alignment on non-clinical supportive information required for EMA submission. We are not in alignment with regard to the comparator agent selected for the cUTI clinical trial and are considering other options to accommodate a European filing for this indication. The EMA may request that we conduct one or more additional clinical trials or non-clinical studies to support potential approval for oral sulopenem and sulopenem for the cUTI indication. We cannot predict how the EMA will interpret the data and results from our Phase 3 clinical trial and other elements of our development program, or whether oral sulopenem or sulopenem will receive any regulatory approvals in the EU.

If we receive regulatory approval for any product candidate, we will be subject to ongoing obligations and continuing regulatory review, which may result in significant additional expense. Our product candidates, including oral sulopenem and sulopenem, if approved, could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if approved.

Any product candidate, including oral sulopenem and sulopenem, for which we obtain marketing approval will also be subject to ongoing regulatory requirements for labeling, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other postmarketing information. For example, approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs. As such, we and our contract manufacturers will be subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and to comply with requirements concerning advertising and promotion for our products.

In addition, even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed, may be subject to significant conditions of approval or may impose requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure that drugs are marketed only for the approved indications and in accordance with the provisions of the approved labelling and regulatory requirements. The FDA also imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not restrict the marketing of our products only to their approved indications, we may be subject to enforcement action for off-label marketing.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us. In addition, if any product fails to comply with applicable regulatory requirements, a regulatory agency may:

- issue fines, warning letters, untitled letters or impose holds on clinical trials if any are still ongoing;
- mandate modifications to promotional materials or require provision of corrective information to healthcare practitioners;
- impose restrictions on the product or its manufacturers or manufacturing processes;
- impose restrictions on the labeling or marketing of the product;
- impose restrictions on product distribution or use;
- require post-marketing clinical trials;
- require withdrawal of the product from the market;
- refuse to approve pending applications or supplements to approved applications that we submit;
- require recall of the product;
- require entry into a consent decree, which can include imposition of various fines (including restitution or disgorgement of profits or revenue), reimbursements for inspection costs, required due dates for specific actions and penalties for non-compliance;
- suspend or withdraw marketing approvals;
- refuse to permit the import or export of the product;
- seize or detain supplies of the product; or
- issue injunctions or impose civil or criminal penalties.

If we fail to comply with federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

As a pharmaceutical company, even though we do not provide healthcare services or receive payments directly from or bill directly to Medicare, Medicaid or other third-party payors for our products, certain federal and state healthcare laws and regulations pertaining to fraud and abuse, patients' rights and other healthcare laws and regulations, are applicable to our business. We are subject to healthcare laws and regulations by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute which prohibits, among other things, any person or entity, from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for either the referral of an individual, or the purchase, lease, furnishing, prescribing, ordering or recommendation of an item, good, facility or service reimbursable by a federally funded healthcare program, such as the Medicare or Medicaid program. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other hand. The term "remuneration" has been interpreted broadly and may constrain our marketing practices, educational programs, pricing policies and relationships with healthcare providers or other entities, among other activities;
- the federal civil and criminal false claims laws, including the federal False Claims Act, and false statement laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other government payors that are false or fraudulent or making any materially false statement in connection with the delivery or payment for healthcare benefits, items or services. Pharmaceutical manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims;
- the Health Insurance Portability and Accountability Act of 1996 (HIPAA), which, among other things, imposes criminal liability for executing or attempting to execute a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and creates federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statements or representations, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry in connection with the delivery of, or payment for, benefits, items or services;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH) and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information, upon certain health plans, healthcare clearinghouses and healthcare providers and their respective business associates that perform services for them involving individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. Among other things, HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- the federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act," and its implementing regulations, which imposes annual disclosure requirements to the CMS on certain manufacturers of drugs, biologics, devices and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions), of certain payments or other transfers of value made to physicians and teaching hospitals, as well as ownership or investment interests held by physicians and their immediate family members;
- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers, which may impose similar or more prohibitive restrictions;
- state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;

- state, local and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, obtain pharmaceutical agent licensure, and/or otherwise restrict payments that may be made to healthcare providers and entities;
- state and local laws that require the registration of pharmaceutical sales representatives; and
- state, local and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to other healthcare providers or entities or marketing expenditures.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Additionally, the Patient Protection and Affordable Care Act (as amended by the Health Care and Education Reconciliation Act), enacted in 2010 (ACA), among other things, amended the intent requirement of the federal Anti-Kickback Statute and criminal health care fraud statutes, so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitute a false or fraudulent claim for purposes of the False Claims Act.

Recently, several pharmaceutical and other healthcare companies have been prosecuted under the federal false claims laws for allegedly inflating drug prices they report to pricing services, which in turn are used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. To the extent that any product we make is sold in a country outside of the United States, we may be subject to similar laws and regulations.

The risks of complying with these laws cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security, fraud and transparency laws is time consuming and costly. If our past or present operations, or those of our distributors are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to sanctions, including civil, criminal and administrative penalties, fines, damages, disgorgement, exclusion from participation in U.S. federal or state health care programs, individual imprisonment, additional reporting obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could materially adversely affect our ability to operate our business and our financial results. Similarly, if healthcare providers, distributors or other entities with whom we do business are found to be out of compliance with applicable laws and regulations, they may be subject to sanctions, which could also have a negative impact on us.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations

In the United States, there have been and continue to be a number of legislative and regulatory changes, and proposed changes, that could affect the future results of our business and operations. In particular, there have been and continue to be a number of initiatives at the federal and states levels that seek to reduce healthcare costs. For example, in March 2010 the ACA was enacted, which has substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. Among the provisions of the ACA, of greatest importance to the pharmaceutical and biotechnology industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price (AMP);
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health program;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- establishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending; and
- implementation of the federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act."

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

S ince enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amendedthe ACA , effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. This decision is under review by the U.S. Supreme Court during its current term. The full effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

In addition, the Centers for Medicare & Medicaid Services, or CMS, has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization (PA) and step therapy (ST) for six protected classes of

drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" while adding a definition of "price concession" in the regulations. It is unclear whether these proposed changes will be accepted, and if so, what effect such changes will have on our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

In addition, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. On December 18, 2019, that court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On January 21, 2020, the U.S. Supreme Court declined to review this decision on an expedited basis. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The costs of prescription pharmaceuticals has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, there has been heightened governmental scrutiny in the United States of the manner in which manufacturers set prices for their marketed products in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. These new laws and initiatives may result in additional reductions in Medicare and other healthcare funding, as well as limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures, all of which could have a material adverse effect on our future customers and accordingly, our financial operations.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Trump administration issued a plan to lower drug prices. Under this blueprint for action, the Trump administration indicated that HHS will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. In addition, on December 23, 2019, the Trump Administration published a proposed rulemaking that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants would be required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, the FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on

certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act, or FCPA, the Irish Criminal Justice (Corruption Offenses) Act 2018, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in that existing laws might be administered or interpreted.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the trade control laws.

There is no assurance that we will be effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA or other legal requirements, including trade control laws. If we are not in compliance with the FCPA and other anti-corruption laws or trade control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the FCPA, other anti-corruption laws or trade control laws by U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

We are subject to various laws protecting the confidentiality of certain patient health information, and our failure to comply could result in penalties and reputational damage. Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union (EU), including personal health data, is subject to the EU General Data Protection Regulation (GDPR), which took effect across all member states of the European Economic Area (EEA), in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data (including health and other sensitive data), including the following: to provide information to individuals regarding data processing activities; to implement safeguards to protect the security and confidentiality of personal data; to make a mandatory breach notification in certain circumstances; and to take certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR

also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater. The GDPR also confers a private right of action on data subjects to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data adding to the complexity of processing personal data in the EU.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the EU. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities, and could lead to government enforcement actions, private litigation and significant fines and penalties against us, all of which could increase our cost of doing business and have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws regarding privacy and security of personal information could expose us to fines and penalties under such laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Our employees, independent contractors, principal investigators, CROs, consultants or vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants or vendors may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA; manufacturing standards; federal and state healthcare fraud and abuse laws and regulations; or laws that require the true, complete and accurate reporting of financial information or data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, additional reporting obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, curtailment of our operations, contractual damages, reputational harm, and diminished potential profits and future earnings, any of which could adversely affect our business, financial condition, results of operations or growth prospects.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our Chief Executive Officer and other key executives and to attract, retain and motivate qualified personnel.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Corey N. Fishman, our Chief Executive Officer, and Michael W. Dunne, M.D., our Chief Scientific Officer, as well as the other principal members of our management, scientific and clinical team. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. We do not maintain "key man" insurance with respect to any of our executive officers or key employees.

If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the

competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

We expect to grow our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, manufacturing, regulatory affairs, sales, marketing and health resources. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Our inability to effectively manage the expansion of our operations may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our potential ability to generate revenue could be reduced and we may not be able to implement our business strategy.

If approvals are obtained outside of the United States, we will be subject to additional risks in conducting business in those markets.

Even if we are able to obtain approval for commercialization of a product candidate in a country outside of the United States, we will be subject to additional risks related to international business operations, including:

- potentially reduced protection for intellectual property rights;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a market outside of the United States (with low or lower prices) rather than buying them locally;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular economies and markets;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting a product candidate and/or finished drug product supply or manufacturing capabilities abroad;
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, hurricanes, typhoons, floods and fires; and
- failure to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act.

These and other risks may materially adversely affect our ability to attain or sustain revenue from markets outside of the United States.

We may engage in acquisitions that could disrupt our business, cause dilution to our shareholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. Any such proposed acquisitions may be subject to the consent of certain holders of the Securities in accordance with the terms and conditions of the Securities as well as the prior written consent of SVB pursuant to the terms of our credit facility with SVB. If we do identify suitable candidates for acquisition, we may not be able to make such acquisitions on favorable terms, or at all, and we may not be able to obtain approval of or consent to such acquisitions from holders of the Securities or SVB. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our ordinary shares or other equity securities to the shareholders of the acquired company, which would reduce the percentage ownership of our then current shareholders. We could incur losses resulting from

undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Taxation

We have been a passive foreign investment company for U.S. federal income tax purposes in the past and we could be a passive foreign investment company in the future, which could subject U.S. Holders to adverse U.S. federal income tax consequences.

We were a passive foreign investment company (PFIC) for U.S. federal income tax purposes for our taxable year ended December 31, 2017.Based on our gross income and average value of our gross assets, we do not believe we (or our wholly owned non-U.S. subsidiary) were a PFIC for the taxable year ended December 31, 2018 or for any subsequent completed taxable year . We do not expect to be a PFIC for the taxable year ending December 31, 2020; however, our status, and the status of our non-U.S. subsidiary, in any taxable year will depend on our assets and activities in that taxable year. As this is a factual determination made annually after the end of each taxable year, there can be no assurances as to our PFIC status for the current taxable year or any future taxable year.

We will be a PFIC in any taxable year if at least (i) 75% of our gross income is "passive income" or (ii) 50% of the average gross value of our assets, determined on a quarterly basis, is attributable to assets that produce, or are held for the production of, passive income. We refer to the passive income test as the "PFIC Income Test" and the asset test as the "PFIC Asset Test".

As used in this section, *Risks Related to Taxation*, the term "U.S. Holder" means a beneficial owner of our ordinary shares that is, for U.S. federal income tax purposes, (1) an individual who is a citizen or resident of the United States, (2) a corporation (or entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof, or the District of Columbia, (3) an estate the income of which is subject to U.S. federal income tax regardless of its source or (4) a trust (x) with respect to which a court within the United States is able to exercise primary supervision over its administration and one or more United States persons have the authority to control all of its substantial decisions or (y) that has elected under applicable U.S. Treasury regulations to be treated as a domestic trust for U.S. federal income tax purposes.

If we are a PFIC in any taxable year in which a U.S. Holder holds shares, subject to the next sentence, we always will be a PFIC with respect to those shares, regardless of the results of the PFIC Income Test or the PFIC Asset Test as applied to us in subsequent taxable years. However, under applicable Treasury regulations, if the preceding sentence applies to a U.S. Holder we will cease to be treated as a PFIC with respect to that U.S. Holder if, in the manner and at the time required by those regulations, the U.S. Holder elects to recognize (and pay tax on, in the manner described in the next paragraph) any unrealized gain in the shares of our stock owned by that U.S. Holder.

If we are a PFIC and a U.S. Holder does not make a mark-to-market election (discussed below) with respect to our ordinary shares, under the so-called "excess distribution" regime that U.S. Holder may be subject to adverse tax consequences, including deferred tax and interest charges, with respect to certain distributions on our ordinary shares, any gain realized on a disposition of our ordinary shares and certain other events. The effect of these tax consequences could be materially adverse to the shareholder. If, in any taxable year during which a U.S. Holder holds our ordinary shares and our non-U.S. subsidiary is a PFIC (i.e., a lower-tier PFIC), such U.S. Holder would be treated as owning a proportionate amount (by value) of the shares of the lower-tier PFIC and would be taxed under the excess distribution regime on distributions by the lower-tier PFIC and on gain from the disposition of shares of the lower-tier PFIC even though such U.S. Holder would not receive the proceeds of those distributions or dispositions.

If a U.S. Holder makes a valid, timely mark-to-market election with respect to our ordinary shares, that U.S. Holder will recognize as ordinary income or loss in each taxable year that we meet the PFIC Income Test or PFIC Asset Test an amount equal to the difference between that U.S. Holder's adjusted basis in our ordinary shares and the fair market value of the ordinary shares, thus also possibly giving rise to phantom income and a potential out-of-pocket tax liability. Ordinary loss generally is recognized only to the extent of net mark-to-market gains previously included in income. U.S. Holders should also be aware that the mark-to-market election generally will not be available with respect to any of our subsidiaries that is a PFIC and that gain recognized on the sale of our ordinary shares that is attributable to a subsidiary that is a PFIC may result in such gain being subject to deferred tax and interest charges.

In certain circumstances a U.S. Holder may make a qualified electing fund, or "QEF election," under the U.S. federal income tax laws with respect to that holder's interest in a PFIC. Such an election may mitigate some of the adverse U.S. federal income tax consequences that could otherwise apply to a U.S. Holder under the excess distribution regime . However, we do not expect to provide U.S. Holders with the information necessary to make a valid QEF election, and such holders should assume that a QEF election will not be available.

If the IRS determines that we are not a PFIC, and a U.S. Holder previously paid taxes pursuant to a mark-to-market election, that holder may have paid more taxes than the holder legally owed.

If the U.S. Internal Revenue Service (IRS) makes a determination that we were not a PFIC in a prior taxable year and a U.S. Holder previously paid taxes pursuant to a mark-to-market election, that U.S. Holder may have paid more taxes than were legally owed due to such election. If such U.S. Holder does not, or is not able to, file a refund claim before the expiration of the applicable statute of limitations, that U.S. Holder will not be able to claim a refund for those taxes.

Changes to U.S. federal income tax laws could have material consequences for us and U.S. Holders of our ordinary shares.

Future U.S. legislation, U.S. Treasury regulations and IRS rulings could affect the U.S. federal income tax treatment of us and U.S. Holders of our ordinary shares, possibly with retroactive effect.

A future transfer of a shareholder's ordinary shares, other than one effected by means of the transfer of book entry interests in DTC, may be subject to Irish stamp duty.

Transfers of our ordinary shares effected by means of the transfer of book entry interests in the Depository Trust Company (DTC) should not be subject to Irish stamp duty. Where the ordinary shares are traded through DTC through brokers who hold such ordinary shares on behalf of customers an exemption should be available because our ordinary shares are traded on a recognized stock exchange in the U.S. However, if a shareholder holds their ordinary shares directly rather than beneficially through DTC through a broker, any transfer of their ordinary shares could be subject to Irish stamp duty (currently at the rate of 1% of the higher of the price paid or the market value of the shares acquired). Payment of Irish stamp duty is generally a legal obligation of the transferee. The potential for stamp duty to arise could adversely affect the price of our ordinary shares.

Dividends paid by us may be subject to Irish dividend withholding tax.

We have never declared or paid cash dividends on our ordinary shares and we do not expect to pay dividends for the foreseeable future. To the extent that we do make dividend payments (or other returns to shareholders that are treated as "distributions" for Irish tax purposes), it should be noted that, in certain limited circumstances, dividend withholding tax (at a rate of 20% prior to December 31, 2019 but increasing to a rate of 25% from January 1, 2020) may arise in respect of dividends paid on our ordinary shares. A number of exemptions from dividend withholding tax exist, such that shareholders resident in EU member states (other than Ireland) or other countries with which Ireland has signed a double tax treaty, which includes the United States, should generally be entitled to exemptions from dividend withholding tax provided that the appropriate documentation is in place. The ability of a U.S. Holder to credit any Irish dividend withholding tax against that U.S. Holder's tentative U.S. federal tax liability may be subject to limitations.

Dividends received by Irish residents and certain other shareholders may be subject to Irish income tax.

We have never declared or paid cash dividends on our ordinary shares and we do not expect to pay dividends for the foreseeable future. To the extent that we do make dividend payments (or other returns to shareholders that are treated as "distributions" for Irish tax purposes), it should be noted that shareholders who are entitled to an exemption from Irish dividend withholding tax on dividends received from us will not be subject to Irish income tax in respect of those dividends, unless they have some connection with Ireland other than their shareholding in Iterum Therapeutics plc (for example, they are resident in Ireland) or they hold their ordinary shares through a branch or agency in Ireland which carries out a trade of their behalf. Shareholders who are not resident nor ordinarily resident in Ireland, but who are not entitled to an exemption from Irish dividend withholding tax, will generally have no further liability to Irish income tax on those dividends which suffer dividend withholding tax.

Our ordinary shares received by means of a gift or inheritance could be subject to Irish capital acquisitions tax.

Irish capital acquisitions tax (CAT) could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares will be regarded as property situated in Ireland. The person who receives the gift or inheritance has primary liability for CAT.

Risks Related to Our Ordinary Shares

An active trading market for our ordinary shares may not be sustained.

Our ordinary shares began trading on the Nasdaq Global Market on May 25, 2018. Given the limited trading history of our ordinary shares, there is a risk that an active trading market for our shares may not be sustained, which could put downward pressure on the market price of our ordinary shares and thereby affect the ability of shareholders to sell their shares. An inactive trading market

for our ordinary shares may also impair our ability to raise capital to continue to fund our operations by issuing shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The price of our ordinary shares has been volatile and could be subject to volatility related or unrelated to our operations and our shareholders' investment in us could suffer a decline in value.

Our share price has been and may continue to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their ordinary shares at or above the price paid for the shares. The trading price of our ordinary shares could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The market price for our ordinary shares may be influenced by those factors discussed elsewhere in this "Risk Factors" section of this document and others, such as:

- results from, and any delays in, our current and future clinical trials, in particular our two ongoing Phase 3 clinical trials related to oral sulopenem and sulopenem;
- announcements of regulatory approval or disapproval of oral sulopenem and sulopenem or future product candidates;
- delays in the commercialization of oral sulopenem and sulopenem or any future product candidates;
- manufacturing and supply issues related to our development programs and commercialization of oral sulopenem and sulopenem or any of our future product candidates;
- quarterly variations in our results of operations or those of our competitors;
- changes in our earnings estimates or recommendations by securities analysts;
- announcements by us or our competitors of new product candidates, significant contracts, commercial relationships, acquisitions or capital commitments;
- announcements relating to future development or license agreements including termination of such agreements;
- adverse developments with respect to our intellectual property rights or those of our principal collaborators;
- commencement of litigation involving us or our competitors;
- changes in our board of directors or management;
- new legislation in the United States relating to the prescription, sale, distribution or pricing of drugs;
- product liability claims, other litigation or public concern about the safety of oral sulopenem or sulopenem or future products;
- market conditions in the healthcare market in general, or in the antibiotics segment in particular, including performance of our competitors; and
- general economic conditions in the United States and abroad.

In addition, the stock market in general, or the market for equity securities in our industry or industries related to our industry, may experience extreme volatility unrelated to our operating performance. These broad market fluctuations may adversely affect the trading price or liquidity of our ordinary shares. Any sudden decline in the market price of our ordinary shares could trigger securities class-action lawsuits against us. If any of our shareholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the time and attention of our management would be diverted from our business and operations. We also could be subject to damages claims if we are found to be at fault in connection with a decline in our share price.

If we fail to maintain compliance with the listing requirements of the Nasdaq Global Market, we may be delisted and the price of our ordinary shares, our ability to access the capital markets and our financial condition could be negatively impacted.

Our ordinary shares are currently listed on the Nasdaq Global Market. To maintain the listing of our ordinary shares on the Nasdaq Global Market, we are required to meet certain listing requirements, including, among others, a minimum closing bid price of $1.00 per share, a market value of publicly held shares (excluding shares held by our officers, directors and 10% or more stockholders) of at least $15 million and a total market value of listed securities of at least $50.0 million.

On March 4, 2020, we received a letter from the Listing Qualifications Department of The Nasdaq Stock Market, LLC notifying us that the listing of our ordinary shares was not in compliance with Nasdaq Listing Rule 5450(b)(2)(A) (MVLS Rule) for continued listing on the Nasdaq Global Market, as the market value of our listed securities was less than $50.0 million for the previous

30 consecutive business days. Under Nasdaq Listing Rule 5810(c)(3)(C), we have a period of 180 calendar days, or until August 31, 2020, to regain compliance with the MVLS Rule. To regain compliance, during this 180-day compliance period, the market value of our listed securities must be at least $50.0 million or more (measured based on closing prices) for a minimum of 10 consecutive business days. In the event that we do not regain compliance with the Nasdaq Listing Rules prior to the expiration of the 180-day compliance period, we will receive written notification from Nasdaq that our securities are subject to delisting. At that time, we may appeal the delisting determination to a hearings panel pursuant to the procedures set forth in the applicable Nasdaq Listing Rules. If we do not regain compliance within the 180-day compliance period, we may also transfer the listing of our ordinary shares to the Nasdaq Capital Market, provided that we then meet the applicable requirements for continued listing on the Nasdaq Capital Market.

There can be no assurance that we will be successful in maintaining the listing of our ordinary shares on the Nasdaq Global Market, or, if transferred, on the Nasdaq Capital Market. This could impair the liquidity and market price of our ordinary shares. In addition, the delisting of our ordinary shares from a national exchange could have a material adverse effect on our access to capital markets, and any limitation on market liquidity or reduction in the price of our ordinary shares as a result of that delisting could adversely affect our ability to raise capital on terms acceptable to us, or at all. The delisting of our ordinary shares from The Nasdaq Stock Market could also negatively impact our financial condition as it would constitute (i) an event of default under the Loan Agreement, which could lead to an acceleration of amounts due under the Loan Agreement and foreclosure upon and/or sale or other liquidation of all of our and our subsidiaries' assets, including intellectual property; and (ii) a fundamental change under the Exchangeable Note Indenture, which could trigger an obligation for us to repurchase the Exchangeable Notes at a repurchase price of 300% of the principal amount of the outstanding Exchangeable Notes.

Through the RLNs, we transferred to the holders thereof rights to receive certain payments in connection with commercial sales of sulopenem, which may reduce our ability to realize potential future revenue from such sales.

As part of the Private Placement, Iterum Bermuda issued RLNs, and in connection with the Rights Offering Iterum Bermuda may issue further RLNs, which entitle the holders thereof to certain payments in connection with commercial sales of sulopenem. Holders of RLNs are entitled to payments based solely on a percentage of our net revenues from U.S. sales of specified sulopenem products (Specified Net Revenues). Payments will be due within 75 days of the end of each six-month payment measuring period (each, a Payment Measuring Period), beginning with the Payment Measuring Period ending June 30, 2020 until (i) the "Maximum Return" (as described below) has been paid in respect of the RLNs, or (ii) the "End Date" occurs, which is December 31, 2045, or (iii) December 31, 2025, in the event that we have not yet received FDA approval with respect to one or more specified sulopenem products by such date. The aggregate amount of payments in respect of all RLNs during each Payment Measuring Period will be equal to the product of total Specified Net Revenues earned during such period and the applicable payment rate (Payment Rate), determined based on which of the specified sulopenem products have received FDA approval. The Payment Rate will be based on the maximum aggregate principal amount of RLNs and will equal (i) up to 15% if we or one of our affiliates has received FDA approval for the use of specified sulopenem products for the treatment of uncomplicated urinary tract infections and (ii) up to 20% if we or one of our affiliates has received FDA approval for the use of specified sulopenem products for the treatment of complicated urinary tract infections but has not received FDA approval for treatment of uncomplicated urinary tract infections.

Prior to the End Date, Iterum Bermuda will be obligated to make payments on the RLNs from Specified Net Revenues until each RLN has received payments equal to $160.00 (or 4,000 times the principal amount of such RLN) (the Maximum Return). The principal amount of the RLNs, equal to $0.04 per RLN, is the last portion of the Maximum Return amount to which payments from Specified Net Revenue are applied . If any portion of the principal amount of the outstanding RLNs has not been paid as of the End Date, Iterum Bermuda must pay the unpaid portion of the principal amount. If Iterum Bermuda fails to pay any amounts on the RLNs that are due and payable, such defaulted amounts will accrue default interest at a rate per annum equal to the prime rate plus three percent (3.00%). Default interest will also accrue on the Principal Amount Multiple (as defined in the RLN Indenture) as a result of certain other defaults under the RLN Indenture at a rate per annum equal to four percent (4.00%).

Iterum Bermuda may at any time redeem for cash all, but not less than all, of the RLNs, at its option. The redemption price per RLN will be equato the Maximum Return for each RLN, less payments made through and including the redemption date, plus certain accrued but unpaid default interest (if any). Upon a change of control of our company, we will require the ultimate beneficial owner or owners controlling the acquiring person or persons to guarantee the obligations of Iterum Bermuda under the RLN Indenture. In the event that a change of control occurs before we receive FDA approval with respect to one or more specified sulopenem products, the redemption price per RLN will be reduced to 50% of the Maximum Return for each RLN, less payments made through and including the redemption date, plus certain accrued but unpaid default interest (if any).

The payment obligations under the RLNs may reduce the revenue we are able to derive from commercial sales of sulopenem and a redemption of the RLNs would require us to use our cash resources, which could adversely affect the value of our company and the prices that investors are willing to pay for our ordinary shares and could adversely affect our business, financial condition and results of operations.

If securities or industry analysts do not publish research or reports about our company, or if they issue adverse or misleading opinions regarding us or our ordinary shares, our share price and trading volume could decline.

The trading market for our ordinary shares relies, in part, on the research and reports that industry or financial analysts publish about our company. If no, or only a few, analysts publish research or reports about our company, the market price for our ordinary shares may be adversely affected. Our share price also may decline if any analyst who covers us issues an adverse or misleading opinion regarding us, our business model, our intellectual property or our share performance, or if our pivotal safety and efficacy studies and operating results fail to meet analysts' expectations. If one or more analysts cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline and possibly adversely affect our ability to engage in future financings.

Our principal shareholders and management own a significant percentage of our ordinary shares and will be able to exert significant control over matters subject to shareholder approval.

Based on shares outstanding as of February 29, 2020, our executive officers, directors, holders of 5% or more of our ordinary shares and their respective affiliates beneficially own in the aggregate approximately 60.6% of our outstanding ordinary shares , not including any ordinary shares issuable upon exchange of any of the Exchangeable Notes purchased by them in the Private Placement. Following the exchange of any of these Exchangeable Notes for ordinary shares, this ownership percentage could increase. As a result of their share ownership, these holders may have the ability to influence our management and policies and will be able to significantly affect the outcome of matters requiring shareholder approval such as elections of directors, amendments of our organizational documents or approvals of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our ordinary shares that our other shareholders may feel are in their best interest.

If these holders , along with the other investors in the Private Placement, including Sarissa, were to exchange their Exchangeable Notes for ordinary shares, based on shares outstanding as of February 29, 2020, such holders and investors in the Private Placement would beneficially own in the aggregate approximately 88.2% of our outstanding ordinary shares.

In addition to the ability to participate generally in shareholder votes to the extent of their ownership of our ordinary shares, pursuant to the 2020 Investor Rights Agreement entered into in connection with the Private Placement, for so long as Sarissa and its affiliates own at least 12.5% of our outstanding ordinary shares on a fully diluted basis, Sarissa will have the right to designate two directors to our board of directors and, for so long as Sarissa and its affiliates own at least 5% but less than 12.5%, Sarissa will have the right to designate one director to our board of directors. Also, some of the other holders of Exchangeable Notes are affiliates of current members of our board of directors. As a result, Sarissa and shareholders affiliated with our directors have significant influence over the election of directors to our board or directors and other matters.

In addition, pursuant to the terms of the 2020 Investor Rights Agreement, for so long as Sarissa owns 10% of our outstanding ordinary shares on a fully diluted basis, Sarissa will have a right of first offer with respect to our future proposed equity financings up to that portion of such new securities which equals Sarissa's percentage ownership of our outstanding ordinary shares on a fully diluted basis, subject to specified exceptions for certain exempt issuances and pursuant to specified procedures. Moreover, Sarissa and other shareholders affiliated with our directors have certain veto rights with respect to negative covenants in the EN Indenture and the RLN Indenture.

As a result of the voting power and board designation rights of these holders, the ability of other shareholders to influence our management and policies could be limited.

If we raise additional capital in the future, our existing shareholders' level of ownership in our Company could be diluted or require us to relinquish rights.

Any issuance of securities we may undertake in the future to raise additional capital could cause the price of our ordinary shares to decline, or require us to issue shares at a price that is lower than that paid by holders of our ordinary shares in the past, which would result in those newly issued shares being dilutive.

Further, if we obtain funds through a debt financing or through the issuance of debt or preference securities, these securities would likely have rights senior to the rights of our ordinary shareholder, which could impair the value of our ordinary shares. Any debt financing we enter into may include covenants that limit our flexibility in conducting our business. We also could be required to seek funds through arrangements with collaborators or others, which might require us to relinquish valuable rights to our intellectual property or product candidates that we would have otherwise retained.

Sales of a substantial number of our ordinary shares in the public market, or the perception that these sales could occur, could cause our share price to fall.

A portion of our outstanding ordinary shares can be traded without restriction at any time. If our current shareholders sell, or indicate an intention to sell, substantial amounts of our ordinary shares in the public market, the trading price of our ordinary shares could decline.

A substantial portion of our outstanding ordinary shares is currently restricted as a result of federal securities laws but can be sold at any time subject to applicable volume limitations. In addition, the Exchangeable Notes that we issued in the Private Placement and the further Exchangeable Notes that we may issue in the Rights Offering are, or may become, exchangeable for our ordinary shares upon the terms and conditions specified therein, and, as set forth in the 2020 Investor Rights Agreement, we have agreed to file a registration statement covering the ordinary shares issuable in connection with the exchange of the Exchangeable Notes, among other securities. Under the 2020 Investor Rights Agreement, we have agreed to file an initial registration statement covering the resale of such securities by the holders thereof within 10 business days following the later of (x) the earlier of (I) the consummation of the Rights Offering and (II) January 21, 2021 and (y) the date on which the number of our unissued ordinary shares available for issuance (less certain reserved shares) is greater than the total number of ordinary shares issuable upon exchange of the then-outstanding Exchangeable Notes . Upon the effectiveness of such registration statement, such shares will be able to be sold by the holders thereof without further restriction.

Furthermore, ordinary shares that are issuable upon exercise of outstanding options, or reserved for future issuance under our equity incentive plans or issuable upon exercise of outstanding warrants will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act. If any of these additional ordinary shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our ordinary shares could decline.

Irish law differs from the laws in effect in the United States and may afford less protection to holders of our securities.

Shareholders may have difficulties enforcing, in actions brought in courts in jurisdictions located outside the United States, judgments obtained in the U.S. courts under the U.S. securities laws. In particular, if a shareholder sought to bring proceedings in Ireland based on U.S. securities laws, the Irish court might consider:

- that it did not have jurisdiction;
- that it was not the appropriate forum for such proceedings;
- that, applying Irish conflict of law rules, U.S. law (including U.S. securities laws) did not apply to the relationship between the shareholder and us or our directors and officers; or
- that the U.S. securities laws were of a penal nature and violated Irish public policy and should not be enforced by the Irish court.

It may not be possible to enforce court judgments obtained in the United States against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is some uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liabilities provisions of the U.S. federal or state securities laws. We have been advised that the United States currently does not have a treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on U.S. federal or state securities laws, would not automatically be enforceable in Ireland.

A judgment obtained against us will be enforced by the courts of Ireland only if the following general requirements are met:

- U.S. courts must have had jurisdiction in relation to the particular defendant according to Irish conflict of law rules (the submission to jurisdiction by the defendant would satisfy this rule); and
- the judgment must be final and conclusive and the decree must be final and unalterable in the court which pronounces it.

A judgment can be final and conclusive even if it is subject to appeal or even if an appeal is pending. But where the effect of lodging an appeal under the applicable law is to stay execution of the judgment, it is possible that in the meantime the judgment may not be actionable in Ireland. It remains to be determined whether final judgment given in default of appearance is final and conclusive. Irish courts may also refuse to enforce a judgment of the U.S. courts which meets the above requirements for one of the following reasons:

- the judgment is not for a definite sum of money;
- the judgment was obtained by fraud;
- the enforcement of the judgment in Ireland would be contrary to natural or constitutional justice;

- the judgment is contrary to Irish public policy or involves certain U.S. laws which will not be enforced in Ireland; or
- jurisdiction cannot be obtained by the Irish courts over the judgment debtors in the enforcement proceedings by personal service in Ireland or outside Ireland under Order 11 of the Irish Superior Courts Rules.

As an Irish company, we are governed by the Irish Companies Act 2014 (the Irish Companies Act), which differs in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company generally are owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our securities may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a jurisdiction of the United States.

Our shareholders should also be aware that Irish law does not allow for any form of legal proceedings directly equivalent to the class action available in the United States.

We have incurred and will incur increased costs as a result of operating as a public company, and our management is required to devote substantial time and attention to our public reporting obligations.

As a publicly-traded company, we have incurred and will continue to incur significant additional legal, accounting and other expenses compared to historical levels. In addition, new and changing laws, regulations and standards relating to corporate governance and public disclosure, including the Dodd-Frank Wall Street Reform and Consumer Protection Act and the rules and regulations promulgated and to be promulgated thereunder, as well as under the Sarbanes-Oxley Act of 2002 (the Sarbanes-Oxley Act), the JOBS Act and the rules and regulations of the U.S. Securities and Exchange Commission (the SEC), and the Nasdaq Global Market, have created uncertainty for public companies and increased our costs and time that our board of directors and management must devote to complying with these rules and regulations. We expect these rules and regulations to increase our legal and financial compliance costs substantially and lead to diversion of management time and attention from revenue-generating activities.

We are an "emerging growth company," and the reduced disclosure requirements applicable to "emerging growth companies" may make our ordinary shares less attractive to investors.

We are an "emerging growth company" as defined in the JOBS Act, and, therefore, we may take advantage of reduced disclosure and regulatory requirements that are otherwise generally applicable to public companies, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments. We may take advantage of these reduced disclosure and regulatory requirements until we are no longer an "emerging growth company." We may remain an "emerging growth company" until as late as December 31, 2023 (the fiscal year-end following the fifth anniversary of our IPO), although we may cease to be an "emerging growth company" earlier under certain circumstances, including if the market value of our ordinary shares that is held by non-affiliates exceeds $700 million as of any June 30, in which case we would cease to be an "emerging growth company" as of the following December 31, or if our gross revenue exceeds $1.07 billion in any fiscal year. In addition, the JOBS Act provides that an emerging growth company can delay adopting new or revised accounting standards until those standards apply to private companies. We have irrevocably elected not to avail ourselves of this delayed adoption of new or revised accounting standards and, therefore, we are subject to the same new or revised accounting standards as public companies that are not emerging growth companies.

The exact implications of the JOBS Act are still subject to interpretations and guidance by the SEC and other regulatory agencies, and we may not be able to take advantage of all of the benefits of the JOBS Act. In addition, investors may find our ordinary shares less attractive if we rely on the exemptions and relief granted by the JOBS Act. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may decline or become more volatile.

If we fail to maintain an effective system of disclosure controls and internal control over financial reporting, our ability to produce timely and accurate financial statements or comply with applicable regulations could be impaired.

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of the applicable listing standards of the Nasdaq Global Market. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Our current controls and any new controls that we develop may become inadequate because of changes in conditions in our business. Further, weaknesses in our disclosure controls and internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective controls or any difficulties encountered in their implementation or

improvement could harm our results of operations or cause us to fail to meet our reporting obligations and may result in a restatement of our consolidated financial statements for prior periods. Any failure to implement and maintain effective internal control over financial reporting could also adversely affect the results of periodic management evaluations and annual independent registered public accounting firm attestation reports regarding the effectiveness of our internal control over financial reporting that we will eventually be required to include in our periodic reports that will be filed with the SEC. Ineffective disclosure controls and procedures and internal control over financial reporting could also cause investors to lose confidence in our reported financial and other information, which would likely have a negative effect on the trading price of our ordinary shares. In addition, if we are unable to continue to meet these requirements, we may not be able to remain listed on the Nasdaq Global Market.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we engaged and continue to engage in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. Additionally, we will be unable to issue securities in the public markets through the use of a shelf registration if we are not in compliance with Section 404.

Any failure to maintain effective disclosure controls and internal control over financial reporting could have a material and adverse effect on our business, results of operations and financial condition and could cause a decline in the trading price of our ordinary shares.

We have never paid cash dividends, do not anticipate paying any cash dividends and our ability to pay dividends, or repurchase or redeem our ordinary shares, is limited by law.

We have never declared or paid cash dividends on our ordinary shares and do not anticipate paying any dividends on our ordinary shares in the foreseeable future. Any determination to pay dividends in the future will be at the sole discretion of our board of directors after considering our financial condition, results of operations, capital requirements, contractual restrictions, general business conditions and other factors our board of directors deems relevant, and subject to compliance with applicable laws, including the Irish Companies Act which requires Irish companies to have distributable reserves available for distribution equal to or greater than the amount of the proposed dividend. Distributable reserves are the accumulated realized profits of the company that have not previously been utilized in a distribution or capitalization less accumulated realized losses that have not previously been written off in a reduction or reorganization of capital. Unless the company creates sufficient distributable reserves from its business activities, the creation of such distributable reserves would involve a reduction of the company's share premium account, which would require the approval of (i) 75% of our shareholders present and voting at a shareholder meeting, and (ii) the Irish High Court. In the event that we do not undertake a reduction of capital to create distributable reserves, no distributions by way of dividends, share repurchases or otherwise will be permitted under Irish law until such time as the company has created sufficient distributable reserves from its business activities. In addition, our ability to pay cash dividends is currently prohibited by the terms of our credit facility with SVB.

Accordingly, the only opportunity for a shareholder to achieve a return on their investment in our company is expected to be if the market price of our ordinary shares appreciates and they sell their ordinary shares at a profit.

Anti-takeover provisions in our Articles of Association and under Irish law could make an acquisition of us more difficult, limit attempts by our shareholders to replace or remove our current directors and management team, and limit the market price of our ordinary shares.

Our Articles contain provisions that may delay or prevent a change of control, discourage bids at a premium over the market price of our ordinary shares, and adversely affect the market price of our ordinary shares and the voting and other rights of the holders of our ordinary shares. These provisions include:

- dividing our board of directors into three classes, with each class serving a staggered three-year term;
- permitting our board of directors to adopt a shareholder rights plan upon such terms and conditions as it deems expedient and in our best interests;
- permitting our board of directors to issue preference shares, with such rights, preferences and privileges as they may designate;

- establishing an advance notice procedure for shareholder proposals to be brought before an annual meeting, including proposed nominations of persons for election to our board of directors; and
- imposing particular approval and other requirements in relation to certain business combinations.

These provisions would apply even if the offer may be considered beneficial by some shareholders. In addition, these provisions may frustrate or prevent any attempts by our shareholders to replace or remove our current management team by making it more difficult for shareholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Provisions in the EN Indenture and RLN Indenture may deter or prevent a business combination that may be favorable to the holders of our ordinary shares.

If a fundamental change occurs prior to the interest record date of the Exchangeable Notes, holders of the Exchangeable Notes will have the right, at their option, to require us to repurchase for cash all or a portion of their Exchangeable Notes. The negative covenants in the EN Indenture also prohibit us from undergoing a change of control transaction, other than a transaction in which each Exchangeable Note holder receives cash consideration of at least 300% of the outstanding principal amount of its notes. Furthermore, the EN Indenture prohibits us from engaging in certain mergers or acquisitions unless , among other things, the surviving entity assumes our obligations under the Exchangeable Notes, the EN Indenture and the guarantees. In addition, the RLN Indenture prohibits us from engaging in certain mergers or acquisitions unless , among other things, the surviving entity assumes our obligations under the RLNs, the RLN Indenture and the guarantees and the RLN Indenture prohibits us from selling, transferring or assigning certain assets and prohibits Iterum Bermuda, the Guarantors or any of our significant subsidiaries from undergoing a change of control, other than in connection with a change of control of us. These and other provisions in the EN Indenture and the RLN Indenture could deter or prevent a third party from acquiring us even when the acquisition may be favorable to the holders of our ordinary shares.

Irish law differs from the laws in effect in the United States with respect to defending unwanted takeover proposals and may give our board of directors less ability to control negotiations with hostile offerors.

Following the authorization for trading of our ordinary shares on the Nasdaq Global Market, we became subject to the Irish Takeover Panel Act, 1997, Irish Takeover Rules 2013 (Irish Takeover Rules). Under the Irish Takeover Rules, our board of directors is not permitted to take any action that might frustrate an offer for our ordinary shares once our board of directors has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of shares, options, restricted share units or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which our board of directors has reason to believe an offer is or may be imminent. These provisions may give our board of directors less ability to control negotiations with hostile offerors than would be the case for a corporation incorporated in a jurisdiction of the United States.

The operation of the Irish Takeover Rules may affect the ability of certain parties to acquire our ordinary shares.

Under the Irish Takeover Rules, if an acquisition of ordinary shares were to increase the aggregate holding of the acquirer and its concert parties to ordinary shares that represent 30% or more of the voting rights of the company, the acquirer and, in certain circumstances, its concert parties would be required (except with the consent of the Irish Takeover Panel) to make an offer for the outstanding ordinary shares at a price not less than the highest price paid for the ordinary shares by the acquirer or its concert parties during the previous 12 months. This requirement would also be triggered by an acquisition of ordinary shares by a person holding (together with its concert parties) ordinary shares that represent between 30% and 50% of the voting rights in the company if the effect of such acquisition were to increase that person's percentage of the voting rights by 0.05% within a 12 month period. Under the Irish Takeover Rules, certain separate concert parties are presumed to be acting in concert. Our board of directors and their relevant family members, related trusts and "controlled companies" are presumed to be acting in concert with any corporate shareholder who holds 20% or more of our shares. The application of these presumptions may result in restrictions upon the ability of any of the concert parties and/or members of our board of directors to acquire more of our securities, including under the terms of any executive incentive arrangements. In the future, we may consult with the Irish Takeover Panel with respect to the application of this presumption and the restrictions on the ability to acquire further securities, although we are unable to provide any assurance as to whether the Irish Takeover Panel will overrule this presumption. Accordingly, the application of the Irish Takeover Rules may restrict the ability of certain of our shareholders and directors to acquire our ordinary shares.

In addition, based on the current exchange rate pursuant to the EN Indenture and assuming physical settlement, we may be required to issue to Sarissa, upon exchange of the Exchangeable Notes it purchased in the Private Placement , ordinary shares representing approximately 22.5% of our fully diluted issue share capital. However, the final number of ordinary shares issuable to Sarissa pursuant to these Exchangeable Notes will depend on the extent to which we elect physical settlement as the exchange method and on the exchange rate at the time of exchange, which may be adjusted pursuant to the terms of the EN Indenture and could result in

our being obligated to issue to Sarissa ordinary shares representing30% or more of our issued voting share capital. While we intend to seek a waiver from the Irish Takeover Panel of any resulting obligation of Sarissa to make a general offer as a result of exchange of these Exchangeable Notes, we cannot be certain that we will be able to obtain such a waiver, and we expect that such a waiver would be conditioned upon the passing of a resolution, on a poll, by our independent shareholders to approve a maximum potential issuance to Sarissa of up to 60% of our ordinary sharesas a result of the exchange of these Exchangeable Notes.

As an Irish public limited company, certain capital structure decisions require shareholder approval, which may limit our flexibility to manage our capital structure.

Under Irish law, our authorized share capital can be increased by an ordinary resolution of our shareholders and the directors may issue new ordinary or preferred shares up to a maximum amount equal to the authorized but unissued share capital, without shareholder approval, once authorized to do so by our Articles of Association or by an ordinary resolution of our shareholders. Additionally, subject to specified exceptions, Irish law grants statutory preemption rights to existing shareholders where shares are being issued for cash consideration but allows shareholders to disapply such statutory preemption rights either in our Articles of Association or by way of special resolution. Such disapplication can either be generally applicable or be in respect of a particular allotment of shares. Accordingly, our Articles of Association contains, as permitted by Irish company law, provisions authorizing the board to issue new shares, and to disapply statutory preemption rights. The authorization of the directors to issue shares and the disapplication of statutory preemption rights must both be renewed by the shareholders at least every five years, and we cannot provide any assurance that these authorizations will always be approved, which could limit our ability to issue equity and thereby adversely affect the holders of our securities.

We do not currently have sufficient authorized share capital or share issuance authorities to convert all of the Exchangeable Notes into ordinary shares, and the number of ordinary shares issuable upon conversion of the Exchangeable Notes could increase.

Under Irish law, a company may only issue shares up to the maximum authorized share capital contained in the company's Constitution. We are currently authorized to issue up to 50,000,000 ordinary shares of $0.01 each, of which 32,698,940 are currently unissued or unreserved and therefore available for issuance. In addition, Irish law requires that the Board of Directors must be authorized by the shareholders in order to issue shares and to dis-apply statutory pre-emption rights. Our Board of Directors is currently authorized to issue up to the amount of our authorized share capital, and to dis-apply the statutory pre-emption right for such issuances. Based on the current exchange rate pursuant to the EN Indenture and assuming physical settlement, our outstanding Exchangeable Notes would exchange into an aggregate of 51,588,000 ordinary shares. In addition, the EN Indenture requires us to increase the exchange rate upon certain events, which would increase the number of ordinary shares deliverable on an exchange. While the Private Placement documents require us to seek and increase of our authorized shares, we can provide no assurances that these approval will be obtained. If such approval is not obtained or we otherwise do not have sufficient authorized shares and share issuance authorities to satisfy our exchange obligations under the Exchangeable Notes, we will be limited to issuing 32,698,940 ordinary shares on conversion of the Exchangeable Notes (regardless of the exchange rate) with the excess being capable of cash settlement only. This could adversely affect our liquidity and/or we may not have sufficient cash available at that time to satisfy such cash settlement. In addition, if such approval is not obtained, we would be limited in our ability to issue equity for other purposes which could adversely affect our shareholders and our ability to raise additional capital.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical and biotechnology companies have experienced significant stock price volatility in recent years. In addition, we may be subject to securities class action litigation as a result of the Private Placement and/or Rights Offering. If we face any such litigation, it could result in substantial costs and a diversion of management's attention and our resources, which could harm our business.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our headquarters are located in Dublin, Ireland, where we lease approximately 5,551 square feet of office space. Our lease extends through November 2026, and we have the option to terminate the lease in November 2021 with one year's notice and a six months' rent penalty. In June 2018 we entered into a lease for a commercial unit in Dublin that extends through June 2038, with the option to terminate the lease in June 2028 with no penalty provided one year's notice is given. We also lease office space in Old Saybrook, Connecticut. Our lease extends through June 2022, and we have the option to extend the term of the lease for such space through June 2025. We also lease office space in Chicago, Illinois. Our lease extends through June 2023, and we have the option to extend the term of the lease for such

space through June 2028. We believe that our current facilities are adequate to meet our near-term needs, and that suitable additional or substitute space will be available as needed on commercially reasonable terms.

Item 3. Legal Proceedings.

From time to time, we may be involved in legal proceedings or be subject to claims arising out of our operations. We are not currently a party to any legal proceedings that in the opinion of our management, would have a material adverse effect on our business.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Shareholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our ordinary shares have been publicly traded on The Nasdaq Global Market under the symbol "ITRM" since May 25, 2018. Prior to that time, there was no public market for our shares.

Holders of Record

On February 29, 2020, we had approximately 18 shareholders of record of our ordinary shares. The actual number of shareholders is greater than this number of record holders and includes shareholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

Dividends

We have never declared or paid cash dividends on our ordinary shares and do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future. Any determination to pay dividends in the future will be at the sole discretion of our board of directors after considering our financial condition, results of operations, capital requirements, contractual restrictions, general business conditions and other factors our board of directors deem relevant, and subject to compliance with applicable laws, including Irish Company law which requires Irish companies to have distributable reserves available for distribution equal to or greater than the amount of the proposed dividend. In addition, our ability to pay cash dividends is currently prohibited by the terms of our credit facility with Silicon Valley Bank.

Recent Sales of Unregistered Securities

From January 1, 2019 through December 31, 2019, we sold and issued the following unregistered securities:

- Pursuant to the terms of a subscription agreement with a supplier, as described in Note 9 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we issued the following ordinary shares on the following dates to the supplier at the respective prices set out below:
    - On July 15, 2019, we issued 17,222 ordinary shares at a price of $6.53 per share for an aggregate subscription price of $0.11 million;
    - On August 19, 2019, we issued 245,493 ordinary shares at a price of $6.79 per share for an aggregate subscription price of $1.67 million;
    - On September 30, 2019, we issued 199,056 ordinary shares at a price of $6.32 per share for an aggregate subscription price of $1.26 million.

Our wholly owned subsidiary, Iterum Therapeutics International Limited, paid the aggregate subscription price for each subscription to us in satisfaction of the supplier's obligation to pay the subscription monies to us and Iterum Therapeutics International Limited's obligation to pay certain amounts due and owing under certain commercial agreements entered into between such subsidiary and the supplier.

The issuances of these securities were exempt from registration under Section 4(a)(2) of the Securities Act (or Regulation D promulgated thereunder) in that the transactions were by an issuer not involving any public offering or were exempt from the registration requirements of the Securities Act in reliance on Regulation S promulgated under the Securities Act on the basis that the shares will not be offered, sold, pledged or transferred in the United States or to a U.S. person for a defined period.

We did not pay or give, directly or indirectly, any commission or other remuneration, including underwriting discounts and commissions, in connection with any of the issuances of securities listed above. All of the foregoing securities were deemed restricted securities for purposes of the Securities Act at the time of issue.

Use of Proceeds from Registered Securities

Not applicable.

Purchases of Equity Securities by the Issuer

None.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes and the other financial information included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a pharmaceutical company dedicated to developing and commercializing sulopenem to be potentially the first and only oral and intravenous (IV) branded penem available globally. Penems, including thiopenems and carbapenems, belong to a class of antibiotics more broadly defined as ß-lactam antibiotics, the original example of which was penicillin, but which now also includes cephalosporins. Sulopenem is a potent, thiopenem antibiotic delivered intravenously which is active against bacteria that belong to the group of organisms known as gram-negatives and cause urinary tract and intra-abdominal infections. We have also successfully developed sulopenem in an oral tablet formulation, sulopenem etzadroxil-probenecid, which we refer to herein as oral sulopenem. Both sulopenem product candidates have the potential to be important new treatment alternatives to address growing concerns related to antibacterial resistance without the known toxicities of some of the most widely used antibiotics, specifically fluoroquinolones. We see two distinct opportunities for our sulopenem program: patients at elevated risk for treatment failure in the community setting suffering from uncomplicated urinary tract infections (uUTI) and hospitalized patients suffering from complicated, antibiotic-resistant infections.

During the third quarter of 2018, we initiated all three clinical trials in our Phase 3 development program which includes: a Phase 3 uUTI clinical trial, known as Sulopenem for Resistant Enterobacteriaceae (SURE) 1, comparing oral sulopenem to oral ciprofloxacin in women with uUTI, a Phase 3 complicated urinary tract infection (cUTI) clinical trial known as SURE 2, comparing IV sulopenem followed by oral sulopenem to IV ertapenem followed by oral ciprofloxacin in adults with cUTI and a Phase 3 complicated intra-abdominal infection (cIAI) clinical trial known as SURE 3, comparing IV sulopenem followed by oral sulopenem to IV ertapenem followed by a combination of oral ciprofloxacin and oral metronidazole in adults with cIAI. We designed one Phase 3 clinical trial in each indication based on our end of Phase 2 meeting with the U.S. Food and Drug Administration (FDA) and feedback from the European Medicines Agency (EMA). We are conducting the Phase 3 clinical trials under Special Protocol Assessment (SPA) agreements from the FDA. We completed enrollment in our uUTI and cUTI clinical trials in the fourth quarter of 2019 and expect to produce topline data around the end of the first quarter of 2020. If these data are positive, we expect to have an opportunity to file two new drug applications (NDAs), one for oral sulopenem and one for IV sulopenem, around mid-2020, which we expect would enable potential FDA approval in the first half of 2021. In December 2019, we announced that sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy for the cIAI trial; however, we believe the secondary supporting analyses and safety data support the potential of sulopenem in the treatment of multi-drug resistant infections. EMA Scientific Advice received by us, consistent with the existing Guidance for this indication, supports an endpoint assessed earlier than the primary study endpoint and a non-inferiority margin of -12.5%.

On May 30, 2018 we completed an initial public offering, or IPO, of our ordinary shares, and issued and sold 6,150,000 ordinary shares at a public offering price of $13.00 per share, resulting in net proceeds of $71.8 million after deducting underwriting discounts and commissions and offering costs payable by us. On June 26, 2018, we issued and sold an additional 200,000 ordinary shares at the IPO price of $13.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional ordinary shares, resulting in additional net proceeds of $2.4 million after deducting underwriting discounts and commissions and offering costs payable by us. Aggregate net proceeds from the IPO totalled $74.2 million after deducting underwriting discounts and commissions and offering costs payable by us.

On July 5, 2019, we filed a universal shelf registration statement on Form S-3 (Registration No. 333-232569) with the SEC, which was declared effective on July 16, 2019, and pursuant to which we registered for sale up to $150.0 million of any combination of our ordinary shares, preferred shares, debt securities, warrants and/or units from time to time and at prices and on terms that we may determine.

On January 21, 2020, we completed a private placement (Private Placement) pursuant to which our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda) issued and sold approximately $51.6 million aggregate principal amount of 6.500% Exchangeable Senior Subordinated Notes due 2025 (Exchangeable Notes) and $0.1 million aggregate principal amount of Limited Recourse Royalty-Linked Subordinated Notes (RLNs and, together with the Exchangeable Notes, the Securities) to a group of accredited investors. The Securities were sold in units (the Units) with each Unit consisting of an Exchangeable Note in the original principal amount $1,000 and 50 RLNs. The Units were sold at a price of $1,000 per Unit. The Exchangeable Notes are exchangeable for our ordinary shares at an initial exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes

(equivalent to an initial exchange price of approximately $1.00 per ordinary share) subject to specified limitations . The RLNs entitle holders to payments based on a percentage of our net revenues from potential U.S. sales of specified sulopenem productssubject to the terms and conditions of the indenture governing the RLNs. Pursuant to the indenture governing the RLNs, the payments on the RLNs will be up to either 15% or 20% of net revenues from U.S. sales of such products, depending on the indication approved by the FDA. The aggregate amount of payments on each RLN is capped at $160.00 (or 4,000 times the principal amount of such RLN). Iterum Bermuda received net proceeds from the sale of the Securities of approximately $46.7 million, after deducting placement agent fees and estimated offering expenses.

Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of oral sulopenem and sulopenem. As of December 31, 2019, we had an accumulated deficit of $234.9 million. We expect to continue to incur significant expenses for the foreseeable future as we advance our sulopenem program through Phase 3 clinical trials, seek regulatory approval and engage in market preparation and pre-commercialization activities. In addition, if we obtain marketing approval for oral sulopenem and sulopenem, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. We are currently evaluating our commercialization strategy in the United States and other territories. We may also incur expenses in connection with the establishment of additional sources for the manufacture of sulopenem tablets and IV vials or the in-license or acquisition of additional product candidates. Additionally, we have incurred and expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

As a result, we will require additional capital to fund our operations, to continue to develop our sulopenem program and to execute our strategy. Until such time as we can obtain marketing approval for oral sulopenem, sulopenem or any future product candidate and generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements, marketing and distribution arrangements or government funding. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of our sulopenem program, or otherwise change our strategy.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2019, we had cash, cash equivalents and restricted cash of $4.9 million. In January 2020, we received net proceeds of approximately $46.7 million from the sale of the Securities. Our expected cash usage for the next 12 months assumes that planned programs and expenditure continue and that we do not reduce or eliminate some or all of our research and development programs or commercialization efforts. Our future viability is dependent on our ability to raise additional capital to finance our operations. Without additional external funding, we do not believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements for the next 12 months . As such, we believe there is substantial doubt about our ability to continue as a going concern for at least one year from the date this Annual Report on Form 10-K is issued. The financial statements do not include any adjustments relating to the recoverability and classification of liabilities that might be necessary should we be unable to continue as a going concern.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of oral sulopenem or sulopenem in the near future . If our development efforts for our sulopenem program are successful and result in regulatory approval and/or license agreements with third parties, we may generate revenue in the future from product sales. To date, all of our revenue has been derived from our Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, award. We expect that our revenue for the foreseeable future will be derived primarily from payments under government awards that we may enter into in the future. In June 2017, CARB-X awarded us funds of up to $1.5 million to advance the development of our sulopenem program. We received funding from CARB-X as we incurred qualifying expenses. During the years ended December 31, 2019, 2018 and 2017 we recognized revenue of $0.0 million, $0.9 million and $0.5 million, respectively, under this award.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the development of our sulopenem program, which include:

- expenses incurred under agreements with contract research organizations (CROs), contract manufacturing organizations (CMOs), as well as investigative sites and consultants that conduct our clinical trials, preclinical studies and other scientific development services;
- manufacturing scale-up expenses and the cost of acquiring and manufacturing preclinical and clinical trial materials and commercial materials, including manufacturing validation batches;
- employee-related expenses, including salaries, related benefits, travel and share-based compensation expense for employees engaged in research and development functions;
- costs related to compliance with regulatory requirements;
- facilities costs, depreciation and other expenses, which include rent under operating lease agreements and utilities; and
- payments made in cash, equity securities or other forms of consideration under third-party licensing agreements.

We expense research and development costs as incurred. Advance payments we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers.

Research and development activities are central to our business model. Product candidates in advanced stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later stage clinical trials. As a result, our research and development expenses increased substantially throughout 2019 as we substantially completed the Phase 3 clinical trials for our sulopenem program, increased personnel costs, including share-based compensation, conducted other clinical trials and prepared regulatory filings for oral sulopenem and sulopenem. This 2019 increase in research and development expenses was partially offset by clinical milestone payments of $15.0 million made to Pfizer in 2018 upon first patient dosing of oral sulopenem and sulopenem in a Phase 3 clinical trial.

The successful development and commercialization of oral sulopenem and sulopenem is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the clinical development of our sulopenem program or when, if ever, material net cash inflows may commence from any of our product candidates. This uncertainty is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the scope, progress, outcome and costs of our clinical trials and other research and development activities;
- successful patient enrollment in, and the initiation and completion of, clinical trials;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- development and timely delivery of commercial drug formulations (i) that can be used in our clinical trials; and (ii) that are available for commercial launch;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- significant and changing government regulation;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our clinical trials, including unexpected topline data of our uUTI and cUTI clinical trials, which we currently expect to report around the end of the first quarter of 2020. For example, in the results of our cIAI clinical trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy for the cIAI trial; however, we believe the secondary supporting analyses and safety data support the potential of sulopenem in the treatment of multi-drug resistant infections. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. Any changes in the outcome of any of these

variables with respect to the development of our product candidates in clinical development could mean a significant change in the costs and timing associated with the development of these product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, related benefits, travel and share-based compensation expense for personnel in executive, finance, market research and administrative functions. General and administrative expenses also include director compensation and travel expenses, insurance, professional fees for legal, patent, consulting, accounting and audit services and market preparation expenses.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support the continued development of our sulopenem program. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance, director compensation, director and officer insurance costs as well as investor and public relations expenses associated with being a public company. Additionally, if and when we believe regulatory approval of oral sulopenem and sulopenem appears likely, we anticipate an increase in payroll and expenses as a result of our preparation for commercial operations.

Interest (Expense) Income, Net

Interest (expense) income, net consists of interest paid and amortization of debt costs on our loan from Silicon Valley Bank (SVB), partially offset by interest earned on our cash and cash equivalents, which are generally invested in money market accounts, as well as interest earned on our investments in marketable securities.

Other Income, Net

Other income, net consists of realized and unrealized gains on our investments in marketable securities, partially offset by realized and unrealized foreign currency gains (losses) incurred in the normal course of business based on movement in the applicable exchange rates.

Provision for Income Taxes

We recognize income taxes under the asset and liability method. Deferred income taxes are recognized for differences between the financial reporting and tax bases of assets and liabilities at enacted statutory tax rates in effect for the years in which the differences are expected to reverse. The effect on deferred taxes of a change in tax rates is recognized in income in the period that includes the enactment date. In evaluating our ability to recover our deferred tax assets, we consider all available positive and negative evidence including past operating results, the existence of cumulative income in the most recent fiscal years, changes in the business in which we operate and our forecast of future taxable income. In determining future taxable income, we are responsible for assumptions utilized including the amount of Irish, U.S. and other foreign pre-tax operating income, the reversal of temporary differences and the implementation of feasible and prudent tax planning strategies. These assumptions require significant judgment about the forecasts of future taxable income and are consistent with the plans and estimates that we are using to manage the underlying business.

Valuation allowances are provided if it is more likely than not that some portion or all of the deferred tax assets will not be realized.

We account for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position. We evaluate our tax positions on a quarterly basis. We also accrue for potential interest and penalties related to unrecognized tax benefits in income tax expense.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors, including central laboratories, in connection with preclinical development activities;
- CROs and investigative sites in connection with preclinical studies and clinical trials; and
- CMOs in connection with drug substance and drug product formulation of preclinical and clinical trial materials.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Share-Based Compensation

We measure share options and other share-based awards granted to employees and directors with service based vesting conditions only based on the fair value on the date of grant using the Black-Scholes option-pricing model. Compensation expense of those awards is recognized over the requisite service period, which is generally the vesting period of the respective award, using the straight-line method.

We measure share-based awards granted to employees and directors with both performance and service based vesting conditions based on the fair value on the date of grant using the Monte Carlo simulation model. Compensation expense of those awards is recognized over the determined vesting period, the period over which all the specified vesting conditions are to be satisfied, using the straight-line method.

For awards granted to consultants and non-employees, compensation expense is recognized over the period during which services are rendered until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of our ordinary shares and updated assumption inputs in the Black-Scholes option-pricing model or the Monte Carlo simulation model.

We classify share-based compensation expense in the consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

The Black-Scholes option-pricing model uses key inputs and assumptions including the expected term of the option, share price volatility, risk-free interest rate, dividend yield, share price and exercise price which is equivalent to closing market value on the date of grant. Many of the assumptions require significant judgment and any changes could have a material impact in the determination of share-based compensation expense.

The Monte Carlo simulation model uses key inputs and assumptions including share price volatility, risk-free interest rate, the expected date of satisfaction of vesting conditions and share price. Many of the assumptions require significant judgment and any changes could have a material impact in the determination of share-based compensation expense.

We have elected to account for forfeitures as they occur.

Determination of the Fair Value of Ordinary Shares prior to IPO

Since our IPO in May 2018, the fair value of our ordinary shares has been determined based on the quoted market price of our ordinary shares. Prior to our IPO, the estimated fair value of our ordinary shares was determined by our board of directors as of the date of each option grant, with input from management, considering our most recently available third-party valuation of our ordinary shares as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation through the date of the grant. Our board of directors considered various objective and subjective factors to determine the fair value of our ordinary shares as of each grant date, including:

- the prices at which we sold preferred shares and the superior rights and preferences of the preferred shares relative to our ordinary shares at the time of each grant;
- the progress of our research and development programs, including the status of preclinical studies and clinical trials for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the pharmaceutical industry and trends within the pharmaceutical industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our ordinary shares and our preferred shares;
- the likelihood of achieving a liquidity event, such as an initial public offering or a sale of our company in light of prevailing market conditions; and
- the analysis of initial public offerings and the market performance of similar companies in the pharmaceutical and biotechnology industries.

Our third-party valuations of ordinary shares were prepared using the option-pricing method (OPM), which used an income and market approach to estimate our enterprise value. The OPM treats ordinary shares and preferred shares as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the ordinary shares have value only if the funds available for distribution to shareholders exceeded the value of the preferred share liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. Discounts for lack of control and marketability of the ordinary shares were applied directly or were inherent in the methodologies employed to arrive at an indication of the value for the ordinary shares.

The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our share-based compensation expense could be materially different.

Results of Operations

Comparison of the Years Ended December 31, 2019 and 2018

The following table summarizes our operating losses for the years ended December 31, 2019 and 2018:

	Year ended December 31,		
	2019	2018	Change
	(In thousands)		
Revenue	$ 37	$ 869	$ (832)
Operating expenses:			
Research and development	90,774	68,647	22,127
General and administrative	11,284	8,781	2,503
Total operating expenses	$ 102,058	$ 77,428	$ 24,630
Operating loss	$ (102,021)	$ (76,559)	$ (25,462)

Revenue

In June 2017, CARB-X awarded us funds of up to $1.5 million to advance the development of our sulopenem program. We received funding from CARB-X as we incurred qualifying expenses. During the years ended December 31, 2019 and 2018, we recognized $0.0 million and $0.9 million of revenue, respectively, under this award. CARB-X funding was fully recognized as of March 31, 2019.

Research and Development Expenses

	Year ended December 31,		
	2019	2018	Change
	(In thousands)		
CRO and other preclinical, clinical trial and milestone related expenses	$ 71,962	$ 41,415	$ 30,547
Personnel related (including share-based compensation)	7,971	8,211	(240)
Chemistry, manufacturing and control (CMC) related expenses	7,560	17,782	(10,222)
Consulting fees	3,281	1,239	2,042
Total research and development expenses	$ 90,774	$ 68,647	$ 22,127

The increase in CRO and other preclinical, clinical trial and milestone related expenses of $30.5 million was primarily due to costs incurred related to our three Phase 3 clinical trials, which initiated in the third quarter of 2018, partially offset by clinical milestone payments of $15.0 million made to Pfizer in 2018 upon first patient dosing of oral sulopenem and sulopenem in a Phase 3 clinical trial. Personnel related expenses decreased by $0.2 million as a result of an increase in the recognition of U.S. and Irish research and development tax credits in 2019, partially offset by an increase in headcount in our CMC, clinical, regulatory and quality functions. Personnel related expenses for the years ended December 31, 2019 and 2018 included share-based compensation expense of $0.7 million and $0.4 million, respectively. CMC related expenses decreased by $10.2 million primarily as a result of the completion of manufacturing of clinical trial materials for our Phase 3 clinical trials in 2018 by our primary suppliers. The increase in consulting fees of $2.0 million was primarily due to an increase in consultants used for clinical trial activity.

General and Administrative Expenses

	Year ended December 31,		
	2019	2018	Change
	(In thousands)		
Personnel related (including share-based compensation)	$ 4,861	$ 4,114	$ 747
Facility related and other	3,308	2,465	843
Professional and consultant fees	3,115	2,202	913
Total general and administrative expenses	$ 11,284	$ 8,781	$ 2,503

Personnel related expenses increased by $0.7 million as a result of an increase in headcount in our general and administrative function. Personnel related expenses for the years ended December 31, 2019 and 2018 included share-based compensation expense of $1.0 million and $0.5 million, respectively. Facility related and other costs increased by $0.8 million primarily as a result of increased lease expenses, increased insurance related costs and higher board of directors compensation. Facility related and other costs for the years ended December 31, 2019 and 2018 included directors' share-based compensation expense of $0.5 million and $0.4 million, respectively. Professional and consulting fees increased by $0.9 million primarily as a result of increased costs associated with operating as a public company.

Comparison of the Years Ended December 31, 2018 and 2017

The following table summarizes our operating losses for the years ended December 31, 2018 and 2017:

	Year ended December 31,		
	2018	2017	Change
	(In thousands)		
Revenue	$ 869	$ 508	$ 361
Operating expenses:			
Research and development	68,647	25,499	43,148
General and administrative	8,781	4,464	4,317
Total operating expenses	$ 77,428	$ 29,963	$ 47,465
Operating loss	$ (76,559)	$ (29,455)	$ (47,104)

Revenue

In June 2017, CARB-X awarded us funds of up to $1.5 million to advance the development of our sulopenem program. We received funding from CARB-X as we incurred qualifying expenses. During the years ended December 31, 2018 and December 31, 2017, we recognized $0.9 million and $0.5 million of revenue under this award.

Research and Development Expenses

	Year ended December 31,		
	2018	2017	Change
	(In thousands)		
CRO and other preclinical, clinical trial and milestone related expenses	$ 41,415	$ 4,665	$ 36,750
Chemistry, manufacturing and control (CMC) related expenses	17,782	15,237	2,545
Personnel related (including share-based compensation)	8,211	3,527	4,684
Consulting fees	1,239	2,070	(831)
Total research and development expenses	$ 68,647	$ 25,499	$ 43,148

The increase in CRO and other preclinical, clinical trial and milestone related expenses of $36.8 million was primarily due to costs incurred related to our three Phase 3 clinical trials, which initiated in the year, as well as an increase in preclinical and Phase 1 clinical trial activity. During 2018, we made clinical milestone payments totaling $15.0 million to Pfizer, upon first patient dosing of oral sulopenem and sulopenem in a Phase 3 clinical trial. These milestone payments were recorded as research and development expenses. CMC related expenses increased by $2.5 million primarily due to process validation activities necessary for our regulatory filings. Personnel related expenses increased by $4.7 million as a result of an increase in headcount in our clinical development, CMC and regulatory functions. Personnel related expenses for the years ended December 31, 2018 and 2017 included share-based compensation expense of $0.4 million and $0.1 million, respectively. The decrease in consulting fees of $0.8 million was primarily due to the increase in employee headcount, reducing our need for outside consultants.

General and Administrative Expenses

	Year ended December 31,		
	2018	2017	Change
	(In thousands)		
Personnel related (including share-based compensation)	$ 4,114	$ 2,463	$ 1,651
Facility related and other	2,465	1,072	1,393
Professional and consultant fees	2,202	929	1,273
Total general and administrative expenses	$ 8,781	$ 4,464	$ 4,317

Personnel related expenses increased by $1.7 million as a result of an increase in headcount in our general and administrative function. Personnel related expenses for the years ended December 31, 2018 and 2017 included share-based compensation expense of $0.5 million and $0.3 million respectively. Facility related and other costs increased by $1.4 million primarily as a result of higher lease charges relating to our offices, increased insurance related costs and higher board of directors compensation. Facility related and other costs for the year ended December 31, 2018 included directors share-based compensation expense of $0.4 million. Professional and consulting fees increased by $1.3 million as a result of pre-commercialization activities.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses and negative cash flows from our operations. We have generated limited revenue to date from a funding arrangement with CARB-X. We have funded our operations to date primarily with proceeds from the sale of preferred shares and ordinary shares, debt raised under our financing arrangement with SVB and payments received under the funding arrangement with CARB-X. Through December 31, 2019, we had received cash proceeds of $198.2 million from sales of our Series A and Series B preferred shares and ordinary shares and $15.0 million from the first drawdown of our SVB loan. As of December 31, 2019, we had cash, cash equivalents, restricted cash and short-term investments of $4.9 million. In January 2020, we received net proceeds of approximately $46.7 million from the sale of units in the Private Placement.

On July 5, 2019, we filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on July 16, 2019, and pursuant to which we registered for sale up to $150.0 million of any combination of our ordinary shares, preferred shares, debt securities, warrants and/or units from time to time and at prices and on terms that we may determine.

As discussed in the Overview in this Management's Discussion and Analysis of Financial Condition and Results of Operations, we believe there is substantial doubt about our ability to continue as a going concern. Should we be unable to adequately finance our business, our results of operations, liquidity and financial condition would be materially and negatively affected, and we

would be unable to continue as a going concern. The financial statements do not include any adjustments relating to the recoverability and classification of liabilities that might be necessary should we be unable to continue as a going concern.

Secured credit facility

On April 27, 2018, our subsidiaries, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited (Borrowers), entered into a Loan and Security Agreement with SVB (Loan Agreement) pursuant to which SVB agreed to lend the Borrowers up to $30.0 million in two term loans. $15.0 million of the secured credit facility was funded on closing. A second draw of up to $15.0 million was available to us through October 31, 2019, upon satisfaction of either of the following: (i) the achievement by us of both non-inferiority and superiority primary endpoints from our Phase 3 uUTI trial, as well as reporting satisfactory safety data from the trial, or (ii) the achievement of non-inferiority primary endpoints from both our Phase 3 uUTI and cUTI trials, as well as reporting satisfactory safety data from the trials. A non-utilization fee of 1.50% of the aggregate undrawn principal amount was to apply if we satisfied the above conditions but chose not to draw down the second term loan. We did not satisfy the conditions for the second draw above before the deadline of October 31, 2019.

Required monthly amortization payments for the initial $15.0 million draw commenced on November 1, 2019 and total principal repayments of $1.0 million were made during the year ended December 31, 2019. Interest accrues at a floating per annum rate equal to the greater of (i) 8.31%; or (ii) 3.89% above the Wall Street Journal prime rate, and is payable monthly in arrears. All outstanding principal, plus a 4.20% final interest payment, will be due and payable on the earliest to occur of March 1, 2022 (the maturity date), the acceleration of either the term loan or the prepayment of the term loan. The final payment fee of $0.6 million, which represents 4.2% of the funded loan, is accreted using the effective interest method over the life of the loan as interest expense. Voluntary prepayments are permitted at any time, subject to a prepayment fee of 4.00% in the first year, 3.00% in the second year, and 2.00% thereafter.

In connection with the initial $15.0 million draw, we issued SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B convertible preferred shares (which converted into warrants to purchase 19,890 ordinary shares upon our IPO) at an exercise price of $18.85 per share. If the second term loan had been drawn down, each of SVB and LSF would have been automatically entitled to purchase additional ordinary shares in an aggregate amount equal to 2.50% of the second term loan divided by the applicable exercise price.

Obligations under the secured credit facility are secured by substantially all of our existing and future assets and the existing and future assets of our subsidiaries, including intellectual property.

In connection with the Private Placement, Iterum Bermuda was joined as a party to the Loan Agreement as a borrower and the Loan Agreement was amended to, among other things, modify the definition of subordinated debt to include the RLNs and Exchangeable Notes.

Cash Flows

The following table summarizes our cash flows for each of the periods presented:

	Year ended December 31,		
	2019	2018	2017
	(In thousands)		
Net cash used in operating activities	$(78,885)	$(75,890)	$(30,604)
Net cash provided by / (used in) investing activities	40,101	(8,658)	(31,587)
Net cash (used in) / provided by financing activities	(974)	120,842	45,867
Effect of exchange rates on cash and cash equivalents	(22)	(108)	—
Net (decrease) / increase in cash	$(39,780)	$36,186	$(16,324)

Operating Activities

During the year ended December 31, 2019, operating activities used $78.9 million of cash, resulting from our net loss of $103.1 million, partially offset by net cash provided by changes in our operating assets and liabilities of $17.9 million and non-cash charges of $6.3 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2019 consisted primarily of increases in accounts payable and accrued expenses, primarily due to increases in clinical trial expenses, and a decrease in prepaid expenses and other current assets, largely related to the use of prepayments previously made to contract research organizations, partially offset by an increase in other assets, primarily related to advance payments to a supplier for equipment, and a decrease in other liabilities as a result of payments made for operating leases.

During the year ended December 31, 2018, operating activities used $75.9 million of cash, resulting from our net loss of $77.1 million and net cash used by changes in our operating assets and liabilities of $1.6 million, partially offset by non-cash charges of $2.8 million. Net cash used by changes in our operating assets and liabilities for the year ended December 31, 2018 consisted primarily of increases in prepaid expenses and other current assets, largely related to advance payments to contract research organizations, and other assets, largely related to a deposit paid for the Dublin commercial lease and advance payments to CMOs, partially offset by increases in accounts payable and accrued expenses, primarily due to an increase in clinical trial expenses

During the year ended December 31, 2017, operating activities used $30.6 million of cash, resulting from our net loss of $29.4 million and net cash used by changes in our operating assets and liabilities of $1.6 million, partially offset by non-cash charges of $0.4 million. Net cash used by changes in our operating assets and liabilities for the year ended December 31, 2017 consisted of increases in prepaid expenses and other assets primarily related to advance payments to CMOs, partially offset by increases in accrued expenses and accounts payable primarily due to increases in clinical trial supply and costs.

Investing Activities

During the year ended December 31, 2019, net cash provided by investing activities of $40.1 million was primarily related to sales of short-term investments. During the year ended December 31, 2018, net cash used in investing activities of $8.7 million was related to purchases of short-term investments of $96.5 million and purchases of property and equipment of $0.1 million, partially offset by sales of short-term investments of $87.9 million. During the year ended December 31, 2017, net cash used in investing activities of $31.6 million was related to purchases of short-term investments of $53.3 million and fixed asset purchases of $0.8 million, partially offset by sales of short-term investments of $22.5 million.

Financing Activities

During the year ended December 31, 2019, net cash used in financing activities of $1.0 million was primarily related to principal repayments made to SVB. During the year ended December 31, 2018, net cash provided by financing activities was $120.8 million and consisted of net cash proceeds from the issuance of Series B-2 preferred shares in February 2018 (which converted to ordinary shares in connection with our IPO) of $32.2 million, net cash proceeds from the issuance of ordinary shares in May and June 2018 associated with our IPO of $74.2 million and net cash proceeds from the SVB loan drawdown of $14.4 million. During the year ended December 31, 2017, net cash provided by financing activities was $45.9 million, and consisted of gross cash proceeds from the issuance of Series B-1 preferred shares in May 2017.

Funding Requirements

We expect to continue to incur significant expenses and increasing operating losses as we conduct our ongoing and planned clinical trials of oral sulopenem and sulopenem, seek marketing approval for such product candidates if clinical trials are successful, and pursue the development of our sulopenem program in additional indications through preclinical and clinical development. Our expenses will also increase substantially if and as we:

- conduct additional clinical trials for oral sulopenem and sulopenem, which include our planned Phase 1 clinical trials related to pediatric indications;
- initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize oral sulopenem and sulopenem in the United States if we obtain marketing approval from the FDA and we choose to commercialize directly in the United States;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of oral sulopenem and sulopenem, if we obtain marketing approval;
- pursue the development of our sulopenem program in additional indications;
- maintain, expand, defend and protect our intellectual property portfolio;
- hire additional clinical, scientific and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our ongoing transition to a public reporting company; and
- acquire or in-license other product candidates or technologies.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical product candidates, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the timing and costs of our ongoing clinical trials of oral sulopenem and sulopenem, including our two ongoing Phase 3 clinical trials;
- the initiation, progress, timing, costs and results of preclinical studies and clinical trials of other potential product candidates and of our current product candidates in additional indications;
- the amount of funding that we receive under government awards that we have applied for or may apply for in the future;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for oral sulopenem and sulopenem and other product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the receipt of marketing approval and revenue received from any potential commercial sales of oral sulopenem and sulopenem;
- the terms and timing of any future collaborations, licensing or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to the Pfizer License or other future license agreements;
- the amount and timing of any payments we are obligated to make in connection with the RLNs;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;
- the costs of operating as a public company; and
- the extent to which we in-license or acquire other products and technologies.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements, marketing and distribution arrangements or government funding. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our shareholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our ordinary shareholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our secured credit facility with SVB, the RLNs and the Exchangeable Notes each impose operating and other restrictions on us. Such restrictions affect, and in many cases limit or prohibit, our ability to dispose of certain assets, pay dividends, incur additional indebtedness, undergo a change of control and enter into certain collaborations, strategic alliances or other similar partnerships, among other things. If we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2019, and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments Due by Period				
	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
	(In thousands)				
Operating lease commitments (1)	$ 6,079	$ 1,099	$ 1,998	$ 1,387	$ 1,595
Principal loan repayments	13,966	6,207	7,759	—	—
Total	$ 20,045	$ 7,306	$ 9,757	$ 1,387	$ 1,595

(1) See note 7 to the consolidated financial statements for further details regarding leases.

Under the Pfizer License, we have agreed to make certain regulatory and sales milestone payments, pay royalties and make a potential one-time payment related to sublicensing income that exceeds a certain threshold. We have not included any contingent payment obligations, such as milestones, royalties, or one-time payments, in the table above as the amount, timing and likelihood of such payments are not known. We are obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage based on marginal net sales of each licensed product.

In June 2016, we entered into an agreement with a supplier whereby we agreed to pay $2.8 million (€2.5 million) to the supplier to acquire equipment, which will be used solely to manufacture product for us. In June 2018, we entered into a supplemental agreement with this supplier whereby we agreed to pay an additional $2.3 million (€2.1 million) for additional equipment and dedicated personnel under the same terms of the original agreement. These payments will be offset against the price of the product to be supplied under a future supply agreement. No balance remained outstanding to the supplier as of as of December 31, 2019.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 permits an “emerging growth company” such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to “opt out” of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission (SEC).

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

As of December 31, 2019, we had cash, cash equivalents of $4.8 million, consisting of cash only. We did not have any marketable securities as of December 31, 2019.

We contract with CROs and CMOs globally. We may be subject to fluctuations in foreign currency rates in connection with certain of these agreements. Transactions denominated in currencies other than the functional currency are recorded based on exchange rates at the time such transactions arise. As of December 31, 2019 and 2018, substantially all of our liabilities were denominated in U.S. dollars. Realized net foreign currency gains and losses did not have a material effect on our results of operations for the years ended December 31, 2019, 2018 and 2017.

The interest rate on our secured credit facility is sensitive to changes in interest rates. Interest accrues at a per annum rate equal to the greater of (i) 8.31%; or (ii) 3.89% above The Wall Street Journal prime rate. The Wall Street Journal prime rate increased from 4.75% to 5.00% on June 14, 2018, to 5.25% on September 27, 2018, to 5.50% on December 20, 2018, and decreased to 5.25% on August 1, 2019, to 5.00% on September 19, 2019 and then to 4.75% on October 31, 2019.

Item 8. Financial Statements and Supplementary Data.

ITERUM THERAPEUTICS PLC

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Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors
Iterum Therapeutics plc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Iterum Therapeutics plc and subsidiaries (the Company) as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, convertible preferred shares and shareholder's (deficit)/equity, and cash flows for each of the years in the three year period ended December 31, 2019, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the years in the three year period ended December 31, 2019, in conformity with U.S. generally accepted accounting principles.

Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered recurring losses from operations and has a net capital deficiency that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company has changed its method of accounting for leases as of January 1, 2019 due to the adoption of ASC Topic 842, Leases.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG

We have served as the Company's auditor since 2015.

Dublin, Ireland
March 12, 2020

ITERUM THERAPEUTICS PLC
Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 4,801	$ 44,551
Short-term investments	—	40,000
Prepaid expenses and other current assets	6,887	8,390
Current portion of restricted cash	30	30
Total current assets	11,718	92,971
Property and equipment, net	572	700
Restricted cash, less current portion	60	90
Other assets	13,401	4,110
Total assets	$ 25,751	$ 97,871
Liabilities and shareholders' (deficit) / equity		
Current liabilities:		
Accounts payable	$ 15,486	$ 4,041
Accrued expenses	12,458	7,046
Current portion of long-term debt	5,800	1,019
Other current liabilities	3,042	—
Income taxes payable	200	113
Total current liabilities	36,986	12,219
Long-term debt, less current portion	7,625	13,079
Other liabilities	7,378	951
Total liabilities	$ 51,989	$ 26,249
Commitments and contingencies *(Note 12)*		
Shareholders' (deficit) / equity:		
Ordinary shares, $0.01 par value per share: 50,000,000 shares authorized, 14,868,973 shares issued at December 31, 2019; 50,000,000 shares authorized, 14,352,046 shares issued at December 31, 2018	149	144
Additional paid-in capital	208,536	203,271
Accumulated deficit	(234,923)	(131,793)
Total shareholders' (deficit) / equity	(26,238)	71,622
Total liabilities and shareholders' (deficit) / equity	$ 25,751	$ 97,871

The accompanying notes are an integral part of these consolidated financial statements.

ITERUM THERAPEUTICS PLC
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Year ended December 31,		
	2019	2018	2017
Revenue	$ 37	$ 869	$ 508
Operating expenses:			
Research and development	(90,774)	(68,647)	(25,499)
General and administrative	(11,284)	(8,781)	(4,464)
Total operating expenses	(102,058)	(77,428)	(29,963)
Operating loss	(102,021)	(76,559)	(29,455)
Interest (expense) / income, net	(861)	(426)	277
Other income, net	196	401	216
Total other (expense) / income	(665)	(25)	493
Loss before income taxes	(102,686)	(76,584)	(28,962)
Income tax expense	(444)	(472)	(444)
Net loss and comprehensive loss	(103,130)	(77,056)	(29,406)
Net loss attributable to ordinary shareholders	$ (103,130)	$ (77,056)	$ (29,406)
Net loss per share attributable to ordinary shareholders – basic and diluted	$ (7.10)	$ (8.82)	$ (170.84)
Weighted average ordinary shares outstanding – basic and diluted	14,518,036	8,734,109	172,130

The accompanying notes are an integral part of these consolidated financial statements.

ITERUM THERAPEUTICS PLC
Consolidated Statements of Convertible Preferred Shares and Shareholders' (Deficit) / Equity
(In thousands, except share and per share data)

	Convertible Preferred Shares		Ordinary Shares		Additional Paid in Capital	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount			
Balance at December 31, 2016	3,032,457	$ 30	413,110	$ 4	$ 47,995	$ (25,331)	$ 22,668
Issuance of Series B convertible preferred shares	2,654,206	27	—	—	45,840	—	45,840
Share-based compensation expense	—	—	—	—	392	—	392
Net loss	—	—	—	—	—	(29,406)	(29,406)
Balance at December 31, 2017	5,686,663	$ 57	413,110	$ 4	$ 94,227	$ (54,737)	$ 39,494
Issuance of Series B convertible preferred shares, net of issuance costs	1,709,650	17	—	—	32,159	—	32,159
Issuance of ordinary shares on initial public offering, net of issuance costs	—	—	6,350,000	64	74,089	—	74,153
Exercise of share options	—	—	2,008	—	7	—	7
Issuance of ordinary shares under subscription agreement	—	—	190,615	2	1,360	—	1,362
Redenomination of share capital	—	42	—	(42)	—	—	(42)
Conversion of preferred shares to ordinary shares	(7,396,313)	(116)	7,396,313	116	—	—	116
Issuance of warrants for ordinary shares	—	—	—	—	139	—	139
Share-based compensation expense	—	—	—	—	1,290	—	1,290
Net loss	—	—	—	—	—	(77,056)	(77,056)
Balance at December 31, 2018	—	$ —	14,352,046	$ 144	$ 203,271	$ (131,793)	$ 71,622
Issuance of ordinary shares in conjunction with vesting of restricted share units	—	—	36,924	—	—	—	—
Exercise of share options	—	—	18,232	—	60	—	60
Issuance of ordinary shares under subscription agreement	—	—	461,771	5	3,032	—	3,037
Share-based compensation expense	—	—	—	—	2,173	—	2,173
Net loss	—	—	—	—	—	(103,130)	(103,130)
Balance at December 31, 2019	—	$ —	14,868,973	$ 149	$ 208,536	$ (234,923)	$ (26,238)

The accompanying notes are an integral part of these consolidated financial statements.

ITERUM THERAPEUTICS PLC
Consolidated Statements of Cash Flows
(In thousands, except share and per share data)

	Year ended December 31,		
	2019	2018	2017
Cash flows from operating activities:			
Net loss	$ (103,130)	$ (77,056)	$ (29,406)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation	152	136	65
Share-based compensation expense	2,173	1,290	392
Gain on short term investments	(125)	(423)	—
Non-cash (gain) / loss on short term investments	—	(278)	44
Interest on short-term investments	(5)	(40)	(95)
Amortization of debt discount and deferred financing costs	362	360	—
Issuance of ordinary shares under subscription agreement	3,037	1,362	—
Other	752	362	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	2,471	(3,613)	(3,815)
Other assets	(1,166)	(2,273)	(782)
Accounts payable	11,446	849	1,671
Accrued expenses	5,851	3,072	1,236
Income taxes	123	120	6
Other liabilities	(826)	242	80
Net cash used in operating activities	(78,885)	(75,890)	(30,604)
Cash flows from investing activities:			
Purchases of property and equipment	(24)	(90)	(812)
Purchases of short-term investments	—	(96,493)	(53,275)
Proceeds from sale of short-term investments	40,125	87,925	22,500
Net cash provided by / (used in) investing activities	40,101	(8,658)	(31,587)
Cash flows from financing activities:			
Proceeds from issuance of debt, net of debt issuance costs	—	14,507	—
Repayments of long-term debt	(1,034)	—	—
Proceeds from issuance of Series A convertible preferred shares	—	—	—
Proceeds from issuance of Series B convertible preferred shares	—	32,175	45,867
Proceeds from issuance of ordinary shares on initial public offering, net of issuance costs	—	74,153	—
Proceeds from exercise of share options	60	7	—
Net cash (used in) / provided by financing activities	(974)	120,842	45,867
Effect of exchange rates on cash and cash equivalents	(22)	(108)	—
Net (decrease) / increase in cash, cash equivalents and restricted cash	(39,780)	36,186	(16,324)
Cash, cash equivalents and restricted cash, at beginning of period	44,671	8,485	24,809
Cash, cash equivalents and restricted cash, at end of period	$ 4,891	$ 44,671	$ 8,485
Supplemental Disclosure of Cash Flow Information:			
Income tax paid—U.S.	$ 414	$ 352	$ 439
Interest paid	1,399	809	—

The accompanying notes are an integral part of these consolidated financial statements.

(1) Nature of Operations and Basis of Presentation

Iterum Therapeutics plc (the "Company") was incorporated under the laws of the Republic of Ireland in June 2015 as a limited company and re-registered as a public limited company on March 20, 2018. The Company maintains its registered office at Block 2 Floor 3, Harcourt Centre, Harcourt Street, Dublin 2, Ireland. The Company commenced operations in November 2015. The Company licensed global rights to its novel anti-infective compound, sulopenem, from Pfizer Inc. ("Pfizer"). The Company is a clinical-stage pharmaceutical company dedicated to developing and commercializing sulopenem to be potentially the first and only oral and intravenous ("IV") branded penem available globally.

Since inception, the Company has devoted substantially all of its efforts to research and development, recruiting management and technical staff, and raising capital, and has financed its operations through the issuance of ordinary and convertible preferred shares, debt raised under a financing arrangement with Silicon Valley Bank ("SVB"), a sub-award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator ("CARB-X") program and the proceeds of a private placement pursuant to which its wholly owned subsidiary, Iterum Therapeutics Bermuda Limited ("Iterum Bermuda") issued and sold approximately $51.6 million aggregate principal amount of 6.500% Exchangeable Senior Subordinated Notes due 2025 ("Exchangeable Notes")and $0.1 million aggregate principal amount of Limited Recourse Royalty-Linked Subordinated Notes (the "RLNs" and, together with the Exchangeable Notes, the "Securities") to a group of accredited investors. The Company has not generated any product revenue. The Company is subject to risks and uncertainties common to early-stage companies in the pharmaceutical industry, including, but not limited to, the ability to secure additional capital to fund operations, failure to successfully develop and commercialize its product candidates, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology and compliance with government regulations. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval prior to commercialization.

Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") and include the accounts of the Company and its subsidiaries.

On May 15, 2018, the Company's shareholders approved a consolidation of its ordinary shares and convertible preferred shares at a 1-for-15.71 ratio (the "Reverse Share Split"), effective on that date. Fractional entitlements to ordinary shares and convertible preferred shares arising as a result of the Reverse Share Split were rounded down to the nearest whole number for each holder of ordinary shares and convertible preferred shares. Those fractional entitlements were aggregated and surrendered to the Company for cancellation. Immediately following the Reverse Share Split, the Company redenominated its ordinary shares and convertible preferred shares from $0.01571 (the nominal value resulting from the Reverse Share Split) per share to $0.01 per share (the "Renominalisation"). All issued and outstanding ordinary shares, convertible preferred shares, options for ordinary shares, restricted share awards, warrants and per share amounts have been retroactively adjusted to reflect this Reverse Share Split and Renominalisation for all periods presented.

On May 30, 2018, the Company completed an initial public offering ("IPO") of its ordinary shares, and issued and sold 6,150,000 ordinary shares at a public offering price of $13.00 per share, resulting in net proceeds of $71.8 million after deducting underwriting discounts and commissions and offering costs payable by the Company. On June 26, 2018, the Company issued and sold an additional 200,000 ordinary shares at the IPO price of $13.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional ordinary shares, resulting in additional net proceeds of $2.4 million after deducting underwriting discounts and commissions and offering costs payable by the Company. Aggregate net proceeds from the IPO totaled $74.2 million after deducting underwriting discounts and commissions and offering costs payable by the Company.

On July 5, 2019, the Company filed a universal shelf registration statement on Form S-3 (Registration No. 333-232569) with the Securities and Exchange Commission ("SEC"), which was declared effective on July 16, 2019, and pursuant to which it registered for sale up to $150.0 million of any combination of its ordinary shares, preferred shares, debt securities, warrants and/or units from time to time and at prices and on terms that the Company may determine.

On January 21, 2020, the Company completed a private placement pursuant to which its wholly owned subsidiary, Iterum Bermuda, issued and sold approximately $51.6 million aggregate principal amount of Exchangeable Notes and $0.1 million aggregate

principal amount of RLNs to a group of accredited investors. The Securities were sold in units (the "Units") with each Unit consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs. The Units were sold at a price of $1,000 per Unit The Exchangeable Notes are exchangeable for the Company's ordinary shares at an initial exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $1.00 per ordinary share), subject to specified limitations . The RLNs entitle holders to payments based on a percentage of the Company's net revenues from potential U.S. sales of specified sulopenem products, subject to the terms and conditions of the indenture governing the RLNs. Pursuant to the indenture governing the RLNs, the payments on the RLNs will be up to either 15% or 20% of net revenues from U.S. sales of such products, depending on the indication approved by the U.S. Food and Drug Administration (the "FDA"). The aggregate amount of payments on each RLN is capped at $160.00 (or 4,000 times the principal amount of such RLN). Iterum Bermuda received net proceeds from the sale of the Securities of approximately $46.7 million, after deducting placement agent fees and estimated offering expenses.

In accordance with Accounting Standards Update ("ASU") 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events, considered in aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year of the date of issue of the consolidated financial statements.

The Company has funded its operations to date primarily with proceeds from the sale of preferred shares and ordinary shares, debt raised under its financing arrangement with SVB, payments received under the CARB-X program and the proceed of a private placement of Exchangeable Notes and RLNs. The Company has incurred operating losses since inception, including net losses of $103,130, $77,056 and $29,406 for the years ended December 31, 2019, 2018 and 2017, respectively. The Company had an accumulated deficit of $234,923 as of December 31, 2019 and expects to continue to incur net losses for the foreseeable future. The Company's future cash flows are dependent on key variables such as its ability to secure additional sources of funding in the form of public or private financing of debt or equity or collaboration agreements.

The Company may not be able to obtain financing on acceptable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's shareholders. If the Company is unable to obtain funding, it could be forced to delay, reduce or eliminate some or all of its research and development programs or commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations. Although management continues to pursue these plans, and the Company has successfully raised capital in the past, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Based on the Company's operating losses since inception, the expectation of continued operating losses for the foreseeable future, and the need to raise additional capital to finance its future operations, management have concluded there is substantial doubt about the Company's ability to continue as a going concern within one year from the date these consolidated financial statements are issued. The accompanying consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

(2) Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual for research and development expenses, the valuation of restricted ordinary shares and the valuation of share-based compensation awards. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates as there are changes in circumstances, facts and experience. Actual results could differ materially from those estimates.

Comprehensive Loss

Comprehensive Loss includes net loss as well as other changes in shareholders' (deficit) / equity that result from transactions and economic events other than those with shareholders. For the periods presented in the accompanying consolidated financial statements, there was no difference between net loss and comprehensive loss.

Consolidation

The accompanying consolidated financial statements include the accounts of Iterum Therapeutics plc and its wholly owned subsidiaries (which are referred to herein, collectively, as the "Company" where context requires). All significant intercompany balances and transactions have been eliminated on consolidation. The Company has no involvement with variable interest entities.

Short-term Investments

The Company classifies short-term investments as available for sale in accordance with the terms of Financial Accounting Standards Board (FASB) Accounting Standard Codification (ASC) 320, *Investments – Debt and Equity Securities.* Realized gains and losses are determined using specific identification. The investments are reported at fair value, with unrealized gains or losses recorded in the consolidated statements of operations and comprehensive loss. Any difference between the cost and fair value of the investments are represented by unrealized gains or losses.

Cash and Cash Equivalents

The Company's cash and cash equivalents consist of cash balances and highly liquid investments with maturities of three months or less at the date of purchase. Accounts held at U.S. financial institutions are insured by the FDIC up to $250, while accounts held at Irish financial institutions are insured under the Deposit Guarantee Scheme up to $112 (€100).

Cash accounts with any type of restriction are classified as restricted cash. If restrictions are expected to be lifted in the next twelve months, the restricted cash account is classified as current. Included within restricted cash on the Company's consolidated balance sheet is a certificate of deposit for $90 which is being held by a third party bank as collateral for the irrevocable letter of credit issued in March 2018 to secure an office lease (see Note 12, Commitments and Contingencies).

Foreign Currencies

Items included in the consolidated financial statements are measured using the currency of the primary economic environment in which the entity operates (functional currency). The consolidated financial statements are presented in U.S. dollars.

Transactions in foreign currencies are recorded at the rate of exchange at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies at the balance sheet date are retranslated into the functional currency at the rate of exchange at the balance sheet date, and the resulting gains and losses are recognized in the consolidated statement of operations and comprehensive loss. Non-monetary items in a foreign currency that are measured in terms of historical cost are translated using the exchange rate at the date of transaction.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated useful life of each asset as follows:

	Estimated Useful Life
Leasehold improvements	Shorter of life of lease or 10 years
Furniture and fixtures	5 years
Laboratory equipment	5 years
Computer equipment	3 years

Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in loss from operations. Repairs and maintenance costs are expensed as incurred. The

Company reviews the recoverability of all long-lived assets, including the related useful life, whenever events or changes in circumstances indicate that the carrying amount of a long-lived asset might not be recoverable.

Leases

The Company determines if an arrangement contains a lease at inception. For arrangements that contain a lease, lease classification, recognition, and measurement are determined at the lease commencement date. The Company has elected to separately account for lease and non-lease components in determining the lease liabilities and right-of-use assets. Lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected lease term. The Company's lease agreements generally do not provide an implicit borrowing rate, therefore the Company uses its incremental borrowing rate at lease commencement to determine the present value of lease payments. The incremental borrowing rate is an entity-specific rate which represents the rate of interest a lessee would pay to borrow on a collateralized basis over a similar term with similar payments. All operating lease expenses are recognized on a straight-line basis over the lease term.

Research and Development Expenses

The Company expenses the cost of research and development as incurred. Research and development expenses comprise costs incurred in performing research and development activities, including salaries, share-based compensation and benefits, facilities costs, depreciation, manufacturing expenses and external costs of third-parties engaged to supply active pharmaceutical ingredient and drug product and conduct preclinical and clinical development activities and trials, as well as the cost of licensing technology, license fees, and other external costs. Advance payments for goods and services that will be used in future research and development activities are recorded as prepaid expenses and expensed when the activity is performed or when the goods have been received.

Accrued Research and Development Expenses

The Company has entered into various research and development contracts with research institutions and other companies. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. This process involves reviewing open contracts and purchase orders, communicating with Company personnel to identify services that have been performed on the Company's behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of actual costs. The majority of the Company's service providers invoice in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. The Company estimates accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known at that time. It periodically confirms the accuracy of these estimates with the service providers and makes adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- Vendors, including central laboratories, in connection with preclinical development activities;
- Clinical Research Organizations, or CROs, and investigative sites in connection with preclinical studies and clinical trials; and
- Contract Manufacturing Organizations, or CMOs, in connection with drug substance and drug product formulation of preclinical and clinical trial materials.

The Company bases expenses related to preclinical studies and clinical trials on estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage preclinical studies and clinical trials on its behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, the accrual or the amount of prepaid expenses is adjusted accordingly. Although the Company does not expect the estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to prior estimates of accrued research and development expenses.

Patent Costs

All patent related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Share-Based Compensation

The Company measures share-based awards granted to employees and directors with service based vesting conditions only based on the fair value on the date of grant using the Black-Scholes option-pricing model. Compensation expense of those awards is recognized over the requisite service period, which is generally the vesting period of the respective award, using the straight-line method.

The Company measures share-based awards granted to employees and directors with both performance and service based vesting conditions based on the fair value on the date of grant using the Monte Carlo simulation model. Compensation expense of those awards is recognized over the determined vesting period, the period over which all the specified vesting conditions are to be satisfied, using the straight-line method.

For awards granted to consultants and non-employees, compensation expense is recognized over the period during which services are rendered until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of the Company's ordinary shares and updated assumption inputs in the Black-Scholes option-pricing model or the Monte Carlo simulation model.

The Company classifies share-based compensation expense in the consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

The Black-Scholes option-pricing model uses key inputs and assumptions including the expected term of the option, share price volatility, risk-free interest rate, dividend yield, share price and exercise price which is equivalent to closing market value on the date of grant. Many of the assumptions require significant judgment and any changes could have a material impact in the determination of share-based compensation expense.

The Monte Carlo simulation model uses key inputs and assumptions including share price volatility, risk-free interest rate, the expected date of satisfaction of vesting conditions and share price. Many of the assumptions require significant judgment and any changes could have a material impact in the determination of share-based compensation expense.

The Company has elected to account for forfeitures as they occur.

Grant Awards

The Company may generate revenue from grant awards that reimburse certain allowable costs for specified projects. For contracts with third parties, when the Company has concluded that it is the principal in conducting the research and development, and where the funding arrangement is considered central to the Company's ongoing operations, it classifies the recognized funding received as revenue.

In June 2017, the Company was granted the CARB-X award in the amount of $1.5 million. The CARB-X award was structured as a cost reimbursement arrangement and was recognized over a period of 20 months from August 2017 to March 2019.

The Company recognized the CARB-X award as revenue, rather than as a reduction of research and development expenses, because the Company was the principal in conducting the research and development activities and this contract was central to its ongoing operations. Revenue was recognized as the qualifying expenses related to the contract were incurred. Five steps are applied in the revenue recognition process: (1) identify the contract with a customer; (2) identify the performance obligation in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligations in the contract; and (5) recognize revenue when (or as) the entity satisfies the performance obligation. Revenue recognized upon incurring qualifying expenses in advance of receipt of funding is recorded in the Company's consolidated balance sheet as other prepaid assets. The related costs incurred by the Company were included in research and development expenses in the Company's consolidated statements of operations and comprehensive loss. The Company recognized $37, $869 and $508 as revenue for the years ended December 31, 2019, 2018 and 2017, respectively, in respect of the CARB-X award.

Research and Development Credits

Research and development credits are available to the Company under the tax laws in both Ireland and the U.S., based on qualifying research and development spend in each jurisdiction as defined under those tax laws. Research and development credits are generally recognized as a reduction of research and development expenses.

Fair Value of Financial Instruments

FASB guidance specifies a hierarchy of valuation techniques based on whether the inputs to those valuation techniques are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurement) and the lowest priority to unobservable inputs (Level 3 measurement).

The three levels of the fair value hierarchy are as follows:

- Level 1 — Unadjusted quoted prices in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date. Level 1 primarily consists of financial instruments whose value is based on quoted market prices such as exchange-traded instruments and listed equities.
- Level 2 — Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly (e.g. quoted prices of similar assets or liabilities in active markets, or quoted prices for identical or similar assets or liabilities in markets that are not active). Level 2 includes financial instruments that are valued using models or other valuation methodologies.
- Level 3 — Unobservable inputs for the asset or liability. Financial instruments are considered Level 3 when their fair values are determined using pricing models, discounted cash flows or similar techniques and at least one significant model assumption or input is unobservable.

The Company's short-term investments and its advance payments to a supplier are carried at fair value, determined according to the fair value hierarchy above, see Note 3 for further details. The carrying amounts reported in the consolidated balance sheets for prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair value based on the short-term maturity of these instruments.

Borrowings

Interest bearing long-term debt is recognized initially at fair value, net of transactions costs incurred. Subsequent to initial recognition, interest bearing long-term debt is measured at amortized cost with any difference between cost and redemption value being recognized as a non-cash component of interest expense in the income statement over the period of the borrowings on an effective interest basis.

Concentration of Credit Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents and short-term investments. The Company has most of its cash and cash equivalents at two accredited financial institutions in the United States, in amounts that exceed federally insured limits. The Company did not hold any short-term investments as of December 31, 2019. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Income Taxes

The Company accounts for income taxes under the asset and liability method which requires deferred tax assets and liabilities to be recognized for the estimated future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, as well as net operating loss carryforwards and research and development tax credits.

Valuation allowances are provided if it is more likely than not that some portion or all of the deferred tax assets will not be realized.

Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. Recognized income tax positions are measured at the largest amount that has a greater than 50% likelihood of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. The Company records interest related to unrecognized tax benefits in interest expense and penalties in general and administrative expenses.

On December 22, 2017, the United States federal government enacted the Tax Act, marking a change from a worldwide tax system to a modified territorial tax system in the United States. As part of this change, the Tax Act, among other changes, provided a reduction of the U.S. federal corporate income tax rate from 34% to 21%, an indefinite carryforward of net operating losses incurred in 2018 and future periods, and an interest limitation starting in 2018 with an indefinite carryforward. Any impact to the Company related to these items was accounted for in the 2017, 2018 and 2019 tax provisions with minimal impact.

Net Loss Per Ordinary Share

Basic and diluted net loss per ordinary share is determined by dividing net loss attributable to ordinary shareholders by the weighted-average ordinary shares outstanding during the period; in accordance with ASC 260, *Earnings per Share.* For the periods presented, the ordinary shares underlying the convertible preferred shares, options, unvested restricted ordinary shares, unvested restricted share units, unvested performance restricted share units and warrants have been excluded from the calculation because they would be anti-dilutive.

The following potentially dilutive securities have been excluded from the computation of diluted weighted-average shares outstanding as they would be anti-dilutive:

	Year ended December 31,		
	2019	2018	2017
Options to purchase ordinary shares	1,150,270	665,219	248,128
Preferred shares convertible into ordinary shares	—	—	5,686,663
Unvested restricted ordinary shares	—	86,068	189,342
Unvested restricted share units	31,367	36,924	—
Unvested performance restricted share units	50,000	—	—
Warrants	19,890	19,890	—
Total	1,251,527	808,101	6,124,133

The weighted-average shares outstanding used to calculate both basic and diluted loss per ordinary share are the same.

Segment and Other Information

The Company determines and presents operating segments based on the information that is internally provided to the Chief Executive Officer, Chief Scientific Officer and Chief Financial Officer, who together are considered the Company's chief operating decision maker, in accordance with ASC 280, *Segment Reporting*. The Company has determined that it operates as a single business segment, which is the development and commercialization of innovative treatments for drug resistant bacterial infections.

The distribution of total operating expenses by geographical area was as follows:

	Year ended December 31,		
Operating expenses	2019	2018	2017
Ireland	$ 90,792	$ 66,552	$ 24,619
U.S.	11,266	10,876	5,344
Total	$ 102,058	$ 77,428	$ 29,963

The distribution of long-lived assets by geographical area was as follows:

Long lived assets	December 31, 2019	December 31, 2018
Ireland	$ 10,936	$ 4,565
U.S.	3,037	245
Total	$ 13,973	$ 4,810

Retirement Plan

The Company has a defined contribution plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all U.S. employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pre-tax basis. If the 401(k) Plan is considered top-heavy at the end of the financial year, with key employee accounts accounting for >60% of total 401(k) Plan assets, the Company is required to contribute a deferral rate of up to 3% to the 401(k) Plan on behalf of certain employees. The Company was not required to make a top-heavy contribution for the year ended December 31, 2019. The Company made contributions of $114 and $33 for the years ended December 31, 2018 and 2017, respectively.

Inventory

Inventories are valued at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method for all inventories. The Company's policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. The estimate of excess quantities is subjective and primarily dependent on the estimates of future demand for a particular product. If the estimate of future demand changes, the Company considers the impact on the reserve for excess inventory and adjusts the reserve as required. Increases in the reserve are recorded as charges in cost of product sales. For product candidates that have not been approved by the FDA, inventory used in clinical trials is expensed at the time of production and recorded as research and development expenses. For products that have been approved by the FDA, inventory used in clinical trials is expensed at the time the inventory is packaged for the clinical trial. Prior to an advisory committee providing a recommendation to the FDA that the Company's application should be approved, costs related to manufacturing the product candidates are recorded as research and development expenses. All direct manufacturing costs incurred after this recommendation will be capitalized into inventory. The Company had no inventory as of December 31, 2019 or December 31, 2018.

Contingent Consideration

Certain license agreements contain milestone payments that could result in the requirement to make contingent consideration payments, see Note 12 for further details. Contingent consideration is recorded at the acquisition date estimated fair value of the contingent payment. The fair value of the contingent consideration is measured at each reporting period. Any related unwinding of discount is recognized as a finance expense. Other changes in fair value are recognized in profit or loss or capitalized as an intangible asset depending on the stage of development. As of December 31, 2019, no milestones had been met that required the Company to recognize contingent consideration.

Recently Adopted Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board (FASB) issued ASU 2016-02,*Leases* (Topic 842) in order to increase transparency and comparability among organizations by recognizing lease assets and lease liabilities on the balance sheet for those leases classified as operating leases under prior GAAP. In July 2018, the FASB issued ASU 2018-11 *Leases* (Topic 842): *Targeted Improvements* which provides the option to adopt the standard retrospectively for each prior period presented, as initially set out in ASU 2016-02, or as of the adoption date with a cumulative-effect adjustment to the opening balance of retained earnings. In March 2019, the FASB issued ASU 2019-03 *Leases* (Topic 842): *Codification Improvements* amending the transition disclosures for Topic 842, in that all companies are exempt from certain interim period transition disclosure requirements.

ASU 2016-02 requires a lessee to recognize a liability to make lease payments (the lease liability) and a right-of-use asset, representing its right to use the underlying asset for the lease term, on the balance sheet. The Company adopted ASU 2016-02 in the first quarter of 2019 utilizing the modified retrospective transition method with an effective date as the date of initial application.

Consequently, prior period balances and disclosures have not been restated. The adoption of ASU 2016-02 on January 1, 2019 resulted in the recognition of right-of-use assets of $7.6 million and operating lease liabilities of $7.8 million, however, the adoption of the standard did not have an impact on the Company's beginning retained earnings, results from operations or cash flows. See Note 7 for further information regarding the impact of the adoption of ASU 2016-02 on the Company's consolidated financial statements.

In July 2017, the FASB issued ASU 2017-11,*Earnings Per Share* (Topic 260), *Distinguishing Liabilities from Equity* (Topic 480), *Derivatives and Hedging* (Topic 815), I. Accounting for Certain Financial Instruments with Down Round Features, II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception.

Part I applies to entities that issue financial instruments such as warrants, convertible debt or convertible preferred shares that contain down-round features. Part II replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. ASU 2017-11 is required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. The adoption of ASU 2017-11 did not have an impact on the Company's consolidated financial statements.

In June 2018, the FASB issued*ASU 2018-07, Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting*

ASU 2018-07 expands the scope of Topic 718 to include all share-based payment transactions for acquiring goods and services from nonemployees. ASU 2018-07 specifies that Topic 718 applies to all share-based payment transactions in which the grantor acquires goods and services to be used or consumed in its own operations by issuing share-based payment awards. ASU 2018-07 also clarifies that Topic 718 does not apply to share-based payments used to effectively provide (1) financing to the issuer or (2) awards granted in conjunction with selling goods or services to customers as part of a contract accounted for under ASC 606. ASU 2018-07 is required to be adopted for annual periods beginning after December 15, 2019, including interim periods within those fiscal years. The adoption of ASU 2018-07 did not have an impact on the Company's consolidated financial statements.

Recent Accounting Pronouncements

There are no recently issued accounting pronouncements that will have a material impact on the Company's consolidated financial statements and related disclosures.

(3) Fair Value of Financial Assets and Liabilities

The following table presents information about the Company's financial assets that were carried at fair value on a recurring basis on the consolidated balance sheet as of December 31, 2019 and December 31, 2018 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value.

December 31, 2019				
Assets	**Total**	**Level 1**	**Level 2**	**Level 3**
Other assets – advance payment to supplier	3,884	—	—	3,884

December 31, 2018				
Assets	**Total**	**Level 1**	**Level 2**	**Level 3**
Short-term investments	$ 40,000	40,000	—	—
Other assets – advance payment to supplier	2,649	—	—	2,649
Total	$ 42,649	40,000	—	2,649

See Note 4 for further details on short-term investments. The other asset above relates to advance payments made to a supplier that were recorded at fair value using the discounted cash flow model, or DCF, as of December 31, 2019 and December 31, 2018. The fair value measurements of these advance payments were determined based on significant unobservable inputs, including a discount rate of 15% and the expected time to recovery of the payment. Changes to the inputs described above are not expected to have a material impact on the company's financial position and results of operations in any given period. See Note 12 — Payments to Supplier, for further details on these advance payments.

The following table presents information about the Company's long-term debt which was carried at amortized cost on the consolidated balance sheet as of December 31, 2019 and December 31, 2018 and indicates the fair value hierarchy of the valuation inputs utilized to determine the approximate fair value.

December 31, 2019

Liabilities	Book Value	Approximate Fair Value	Level 1	Level 2	Level 3
Current portion of long-term debt	$ 5,800	$ 5,800	—	5,800	—
Long-term debt, less current portion	7,625	7,213	—	7,213	—
Total	$ 13,425	$ 13,013	—	13,013	—

December 31, 2018

Liabilities	Book Value	Approximate Fair Value	Level 1	Level 2	Level 3
Current portion of long-term debt	$ 1,019	$ 1,019	—	1,019	—
Long-term debt, less current portion	13,079	13,035	—	13,035	—
Total	$ 14,098	$ 14,054	—	14,054	—

The book value of the current portion of long-term debt approximates its fair value due to the short-term nature of the balance. The fair value of long-term debt, less current portion was determined based on a DCF analysis using quoted market interest rates, without consideration of transaction costs, which represents a Level 2 basis of fair value measurement. The counterparty to the long-term debt is a major international financial institution.

The carrying amounts reported in the consolidated balance sheets for prepaid expenses and other current assets, accounts payable, accrued expenses and other current liabilities approximate their fair value based on the short-term maturity of these instruments.

There have been no transfers of assets or liabilities between the fair value measurement levels.

(4) Short-term Investments

The Company classifies its short-term investments as available for sale. Short-term investments comprise highly liquid investments with minimum "A-" rated securities. Investments are reported at fair value with unrealized gains or losses recorded in the consolidated statements of operations and comprehensive loss. Any differences between the cost and fair value of investments are represented by unrealized gains or losses. The fair values of short-term investments are represented by Level 1 fair value measurements – quoted prices in active markets for identical assets.

The Company did not hold any short-term investments as of December 31, 2019. The following table represents the Company's available for sale short-term investments by major security type as of December 31, 2018:

December 31, 2018

Available for sale	Cost Total	Unrealized gains	Unrealized (losses)	Fair Value Total	Maturity by period: Less than 1 year	Maturity by period: 1 to 5 years
Commercial paper	$ 35,745	272	(9)	36,008	36,008	—
U.S. Treasury and Agency Bonds	3,977	15	—	3,992	3,992	—
Total	$ 39,722	287	(9)	40,000	40,000	—

(5) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following:

	December 31, 2019	December 31, 2018
Deferred financing expenses (1)	$ 2,339	—
Prepaid research and development expenses	1,679	5,351
Short-term deposits	1,139	959
Research and development tax credit receivable	1,036	404
Prepaid insurance	569	438
Value added tax receivable	68	159
Other prepaid assets	50	921
Interest receivable	7	158
Total	$ 6,887	$ 8,390

(1) See note 15 to the consolidated financial statements for further details deferred financing expenses.

(6) Property and Equipment, net

Property and equipment and related accumulated depreciation are as follows:

	December 31, 2019	December 31, 2018
Leasehold improvements	$ 592	$ 592
Furniture and fixtures	120	120
Laboratory equipment	81	81
Computer equipment	132	108
	925	901
Less: accumulated depreciation	(353)	(201)
	$ 572	$ 700

Depreciation expense was $152, $136 and $65 for the years ended December 31, 2019, 2018 and 2017, respectively.

(7) Leases

The Company has entered into a number of operating leases, primarily for office space and commercial property. These leases have terms which range from four to 19 years, and generally include one or more options to terminate or renew. The termination options can reduce the lease term for periods ranging from five to 10 years, however the remaining lease terms do not represent these early termination dates as management has concluded that it is reasonably certain that the Company will not exercise these options. The renewal terms can extend the lease term for additional periods ranging from three to five years. These renewal options are represented in the remaining lease term as management has concluded that it is reasonably certain that the Company will exercise the renewal option. Certain leases contain variable lease payments, including payments based on an index or rate. Variable lease payments based on an index or rate are initially measured using the index or rate in effect at lease commencement. Certain agreements contain both lease and non-lease components. The Company has elected to separately account for these components in determining the lease liabilities and right-of-use assets. The Company's lease agreements generally do not provide an implicit borrowing rate, therefore an internal incremental borrowing rate was determined based on information available at lease commencement date for the purposes of determining the present value of lease payments. The Company used the incremental borrowing rate on January 1, 2019 for all leases that commenced prior to that date. All operating lease expenses are recognized on a straight-line basis over the lease term. The Company recognized $1,015 of operating lease costs for right-of-use assets during the year ended December 31, 2019.

Information related to the Company's right-of-use assets and related lease liabilities is as follows:

	Year Ended December 31, 2019
Cash paid for operating lease liabilities	$ 826
Right-of-use assets obtained in exchange for new operating lease obligation(1)	7,622

(1) All operating lease included above were held at January 01, 2019.

	December 31, 2019
Weighted-average remaining lease term	12.5 years
Weighted-average discount rate	7.6%

Right-of-use assets and lease liabilities for the Company's operating leases were recorded in the consolidated balance sheet as follows, representing the Company's right to use the underlying asset for the lease term ("Other assets") and the Company's obligation to make lease payments ("Other current liabilities" and "Other liabilities"):

	December 31, 2019
Other assets	$7,144
Other current liabilities	$580
Other liabilities	6,748
Total lease liabilities	$7,328

The Company has recorded the reduction in carrying amount of the right-of-use assets and the change in the lease liability in the Other category within the operating section of the consolidated statement of cash flows.

Future lease payments included in the measurement of lease liabilities on the consolidated balance sheet as of December 31, 2019 for the following five fiscal years and thereafter were as follows:

Due in 12 month period ended December 31,	
2020	$1,099
2021	1,023
2022	1,032
2023	1,038
2024	1,042
Thereafter	5,641
	$10,875
Less imputed interest	(3,547)
Total lease liabilities	$7,328

As of December 31, 2018, future minimum lease payments, as defined under the previous lease accounting guidance of ASC Topic 840, under non-cancelable operating leases for the following five fiscal years and thereafter were as follows:

Due in 12 month period ended December 31,	
2019	$904
2020	1,020
2021	1,030
2022	985
2023	766
Thereafter	2,356
	$7,061

(8) Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2019	December 31, 2018
Accrued clinical trial costs	$ 9,866	$ 2,849
Accrued payroll and bonus expenses	1,207	1,804
Accrued manufacturing expenses	136	1,439
Accrued other expenses	1,249	954
Total	$ 12,458	$ 7,046

(9) Shareholders' (Deficit) / Equity

The Company's capital structure consists of ordinary shares, undesignated preferred shares and, prior to the completion of the Company's IPO on May 30, 2018, convertible preferred shares with certain rights and privileges summarized below. Under Irish law, the Company is prohibited from allotting shares without consideration. Accordingly, at least the nominal value of the shares issued underlying any restricted share award, restricted share unit, performance share award, bonus share or any other share based grant must be paid pursuant to the Irish Companies Act 2014 ("Irish Companies Act").

Ordinary Shares

The Company was initially incorporated without a cap on its authorized share capital as permitted by the Irish Companies Act. On October 14, 2015, the Company authorized and issued 413,110 ordinary shares with a par value of $0.01 per share (after taking account of the reverse share split and redenomination of the par value of the ordinary shares from $0.01571 (the nominal value resulting from the reverse share split) to $0.01 on May 15, 2018). On March 13, 2018, the Company redenominated its 44,557,606 authorized and 413,110 issued ordinary shares from $0.0001 to $0.001 per share in accordance with section 83(1)(c) of the Irish Companies Act.

On November 18, 2015, the Company increased the authorized ordinary share capital to 3,659,453 shares with a par value of $0.01 per share.

On May 18, 2017, the Company increased the authorized ordinary share capital to 7,956,715 shares with a par value of $0.01 per share.

On February 16, 2018, the Company increased its authorized ordinary shares by 36,600,891 to 44,557,606 ordinary shares with a par value of $0.01 per share.

On May 30, 2018, the Company increased its authorized ordinary shares by 5,442,394 to 50,000,000 ordinary shares of $0.01 each.

On December 14, 2018, Iterum Therapeutics plc ("ITP") and Iterum Therapeutics International Limited ("ITIL") entered into a subscription agreement with a supplier of ITIL pursuant to which the supplier agreed to subscribe for ordinary shares in ITP in satisfaction of amounts due and owing under certain commercial agreements entered into between the supplier and ITIL (the "Subscription Agreement"). Pursuant to the terms of the Subscription Agreement, upon receipt by ITIL of a valid invoice from the supplier, ITP can elect to require the supplier to subscribe for ordinary shares in the capital of ITP (up to a maximum of 700,000 ordinary shares in total) to the value of the invoiced amount (a "Subscription"). On a Subscription, the supplier will direct ITIL to pay ITP such invoiced amount as subscription monies on the supplier's behalf in satisfaction of the invoiced amount.

On December 14, 2018, ITP elected that the supplier subscribe for 190,615 ordinary shares for an aggregate subscription price of $1.36 million (the "December Subscription Monies") upon receipt by ITIL of valid invoices up to that amount from the supplier (the "Invoiced Amount"). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $1.36 million (€1.20 million) to ITP in satisfaction of the supplier's obligation to pay the December Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

On July 15, 2019, ITP elected that the supplier subscribe for 17,222 ordinary shares for an aggregate subscription price of $0.11 million (the "July Subscription Monies") upon receipt by ITIL of valid invoices up to that amount from the supplier (the "Invoiced Amount"). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $0.11 million (€0.10 million) to ITP in satisfaction of the supplier's obligation to pay the July Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

On August 19, 2019, ITP elected that the supplier subscribe for 245,493 ordinary shares for an aggregate subscription price of $1.67 million (the "August Subscription Monies") upon receipt by ITIL of valid invoices up to that amount from the supplier (the "Invoiced Amount"). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $1.67 million (€1.50 million) to ITP in satisfaction of the supplier's obligation to pay the August Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

On September 30, 2019, ITP elected that the supplier subscribe for 199,056 ordinary shares for an aggregate subscription price of $1.26 million (the "September Subscription Monies") upon receipt by ITIL of valid invoices up to that amount from the supplier (the "Invoiced Amount"). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $1.26 million (€1.15 million) to ITP in satisfaction of the supplier's obligation to pay the September Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

The holders of ordinary shares are entitled to one vote for each share held. The holders of ordinary shares have no preemptive or other subscription rights, and there are no redemption or sinking fund provisions with respect to such shares.

Undesignated Preferred Shares

On May 30, 2018, the Company created a new class of undesignated preferred shares of $0.01 each, 100,000,000 of which were authorized immediately prior to closing of the initial public offering. The Directors are authorized by the Company's Articles of Association to determine the rights attaching to the undesignated preferred shares including rights of redemption, rights as to dividends, rights on winding up and conversion rights. There were no undesignated preferred shares in issue as of December 31, 2019 or December 31, 2018.

Convertible Preferred Shares

On November 18, 2015, the Company authorized 3,022,915 Series A convertible preferred shares with a par value of $0.01 per share. On the same day, the Company issued 1,514,320 Series A convertible preferred shares for a purchase price of $15.71 per share for: (1) gross cash proceeds of $20,701; (2) the issue of 190,961 convertible preferred shares to Pfizer as part consideration for the license agreement; and (3) the conversion of $90 debt owed by the Company to its founders for a total of 5,728 preferred shares (after taking account of the reverse share split and redenomination of the par value of the convertible preferred shares from $0.01571 (the nominal value resulting from the reverse share split) per share to $0.01 on May 15, 2018). On March 13, 2018, the Company redenominated its 3,032,463 authorized and 3,032,457 issued Series A convertible preferred shares from $0.0001 to $0.001 par value per share in accordance with section 83(1)(c) of the Irish Companies Act.

On December 9, 2016, the Company authorized 9,548 Series A convertible preferred shares with a par value of $0.01 per share.

On December 16, 2016, the Company issued 1,518,137 Series A convertible preferred shares for a purchase price of $15.71 per share for: (1) gross cash proceeds of $20,851; and (2) the issue of an additional 190,961 convertible preferred shares to Pfizer as part consideration for the license agreement.

On May 18, 2017, the Company authorized 2,654,215 Series B-1 convertible preferred shares with a par value of $0.01 per share and 1,042,728 Series B-2 convertible preferred shares with a par value of $0.01 per share (the "Series B convertible preferred shares"). On the same day, the Company issued 2,654,206 Series B-1 convertible preferred shares for a purchase price of $17.28 per share, for gross cash proceeds of $45,867 (after taking account of the reverse share split and redenomination of the par value of the convertible preferred shares from $0.01571 (the nominal value resulting from the reverse share split) per share to $0.01 on May 15, 2018). On March 13, 2018, the Company redenominated its 4,801,493 authorized and 4,363,856 issued Series B convertible preferred shares from $0.0001 to $0.001 par value per share in accordance with section 83(1)(c) of the Irish Companies Act.

On February 16, 2018, the Company increased its authorized Series B-2 convertible preferred shares to 2,147,278 shares with a par value of $0.01 per share. On the same day, the Company issued 1,709,650 Series B-2 convertible preferred shares for consideration of $18.85 per share, for gross cash proceeds of $32,230.

On May 30, 2018, immediately prior to the completion of the Company's IPO, holders of convertible preferred shares of Iterum Therapeutics Plc exchanged their preferred shares for ordinary shares of Iterum Therapeutics Plc on a one-for-one basis and all convertible preferred shares were subsequently cancelled.

Prior to the exchange and cancellation of preferred convertible shares on May 30, 2018, the ordinary shares were subordinate to the convertible preferred shares with respect to dividend rights and rights upon liquidation, winding up and dissolution of the Company and the holders of ordinary shares were entitled to liquidation proceeds after all liquidation preferences for the convertible preferred shares were satisfied.

(10) Share-Based Compensation

On November 18, 2015, the Company's Board of Directors adopted and approved the 2015 Equity Incentive Plan (the "2015 Plan"), which authorized the Company to grant up to 223,424 ordinary shares in the form of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units and other share awards. The types of share-based awards, including the rights amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors. The purpose of the 2015 Plan is to provide the Company with the flexibility to issue share-based awards as part of an overall compensation package to attract and retain qualified personnel. On May 18, 2017, the Company amended the 2015 Plan to increase the number of ordinary shares available for issuance under the 2015 Plan by 219,605 shares to 443,029 shares.

On March 14, 2018, the Company's Board of Directors adopted and approved the 2018 Equity Incentive Plan (the "2018 Plan"), which became effective upon the execution and delivery of the underwriting agreement related to the Company's IPO. No further grants will be made under the 2015 Plan. The ordinary shares underlying any options that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2015 Plan will not be added back to the ordinary shares available for issuance.

The 2018 Plan authorizes the Company to grant up to 1,018,459 ordinary shares in the form of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units, performance share awards, performance cash awards and other share awards. The types of share-based awards, including the amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors. The ordinary shares underlying any options that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2018 Plan will be added back to the ordinary shares available for issuance under the 2018 Plan.

On December 5, 2018, pursuant to powers delegated to it by the Board of Directors of the Company, the Compensation Committee approved an increase in the number of ordinary shares available to be granted pursuant to the 2018 plan by 4% of the total number of shares of the Company's issued share capital on December 31, 2018, being 574,081 ordinary shares.

Restricted Ordinary Shares

In connection with the Company's formation, 413,110 restricted ordinary shares were issued on October 14, 2015 to the Company's founders at par value. These ordinary shares are subject to various restrictions pursuant to ordinary share purchase agreements between the Company and each founder, including restrictions on transfer and a Company right of repurchase. The restricted ordinary shares were 25% vested as of October 14, 2016 and 1/36th of the remaining restricted ordinary shares vested on a monthly basis thereafter (subject to acceleration of vesting in connection with certain change of control transactions). A change in status occurred on November 18, 2015 when the founders became employees of the Company. The grant date of these shares is now considered to be November 18, 2015 when the fair value was $3.14 per share.

The Company records share-based compensation expense for the restricted ordinary shares based on the grant date fair value. The Company recorded an expense of $260, $332 and $333 for the years ended December 31, 2019, 2018 and 2017, respectively. There was no unamortized compensation expense related to restricted ordinary shares as of December 31, 2019. Total unamortized compensation expense related to restricted ordinary shares was $260 and $592 as of December 31, 2018 and December 31, 2017, respectively, and was recognized over a weighted average period of 0.79 years and 1.79 years.

A summary of the Company's restricted ordinary share activity and related information is as follows:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested at December 31, 2016	292,620	$ 3.14
Granted	—	
Vested	(103,278)	$ 3.14
Forfeited	—	
Unvested at December 31, 2017	189,342	$ 3.14
Granted	—	
Vested	(103,274)	$ 3.14
Forfeited	—	
Unvested at December 31, 2018	86,068	$ 3.14
Granted	—	
Vested	(86,068)	$ 3.14
Forfeited	—	
Unvested at December 31, 2019	—	$ 3.14

Share Options

Unless specified otherwise in an individual option agreement, share options granted under the 2015 Plan and the 2018 Plan generally have a ten year term and a four year vesting period. The vesting requirement is conditioned upon a grantee's continued service with the Company during the vesting period. Once vested, all awards are exercisable from the date of grant until they expire. The option grants are non-transferable. Vested options generally remain exercisable for 90 days subsequent to the termination of the option holder's service with the Company. In the event of an option holder's disability or death while employed by or providing service to the Company, the exercisable period extends to twelve months or eighteen months, respectively.

The fair value of options granted during the years ended December 31, 2019, 2018 and 2017 was estimated using the Black-Scholes option-pricing model. The inputs for the Black-Scholes model require management's significant assumptions. The risk-free interest rate was based on a normalized estimate of the 7-year U.S. treasury yield. The Company has estimated the expected term utilizing the "simplified" method for awards that qualify as "plain vanilla". The Company does not have sufficient company-specific historical and implied volatility information and it therefore estimates its expected share volatility based on historical volatility information of reasonably comparable guideline public companies and itself. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price. Expected dividend yield is based on the fact that the Company has never paid cash dividends, its ability to pay cash dividends is currently prohibited by the terms of its credit facility with SVB and the Company's future ability to pay cash dividends on its shares may be limited by the terms of any future debt or preferred securities. The Company has elected to account for forfeitures as they occur.

The Company granted 512,778, 479,986 and 198,798 share options to employees and directors during the years ended December 31, 2019, 2018 and 2017, respectively. There were 837,386, 566,813 and 228,809 unvested employee and director options outstanding as of December 31, 2019, December 31, 2018 and December 31, 2017, respectively. Total expense recognized related to the employee and director share options was $1,388, $669 and $59 for the years ended December 31, 2019, 2018 and 2017, respectively. Total unamortized compensation expense related to employee and director share options was $3,342, $2,822 and $396 as of December 31, 2019, December 31, 2018 and December 31, 2017, respectively, expected to be recognized over a remaining weighted average vesting period of 2.61 years, 3.07 years and 3.51 years as of December 31, 2019, December 31, 2018 and December 31, 2017, respectively.

The range of assumptions that the Company used to determine the grant date fair value of employee and director options granted were as follows:

	Year ended December 31,		
	2019	2018	2017
Volatility	68.9 - 74.5%	60%	60%
Expected term in years	5.50 - 6.25	6.25	6.25
Dividend rate	0%	0%	0%
Risk-free interest rate	1.73 - 2.57%	2.16 - 2.91%	1.63%
Share price	3.55 - 6.80	7.06 - 13.00	3.30 - 4.40
Fair value of option on grant date	2.37 - 4.41	4.41 - 7.49	1.88 - 2.50

The following table summarizes the number of options outstanding and the weighted-average exercise price:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value (in thousands)
Options outstanding December 31, 2016	49,330	$ 3.14	8.51	
Granted	198,798	$ 3.36		
Options outstanding December 31, 2017	248,128	$ 3.31	9.44	
Granted	479,986	$ 12.60		
Exercised	(2,008)	$ 3.30		
Forfeited	(60,887)	$ 10.99		
Options outstanding December 31, 2018	665,219	$ 9.31	8.93	395
Granted	512,778	$ 5.94		
Exercised	(18,232)	$ 3.29		
Forfeited	(8,726)	$ 7.43		
Expired	(769)	$ 6.77		
Options outstanding December 31, 2019	1,150,270	$ 7.92	8.59	254
Exercisable at December 31, 2019	312,884	$ 8.82	8.02	157

The aggregate intrinsic value of share options is calculated as the difference between the exercise price of the share options and the fair value of the Company's ordinary shares for those share options that had exercise prices lower than the fair value of the Company's ordinary shares as of December 31, 2019 and December 31, 2018.

The weighted average grant-date fair value per share of share options granted during the years ended December 31, 2019, 2018 and 2017 was $3.80, $7.25 and $1.91, respectively.

Restricted Share Units (RSUs)

The Company granted 31,367 and 36,924 RSUs to directors during the years ended December 31, 2019 and 2018, respectively. No RSUs were granted prior to the year ended December 31, 2018.

The table below shows the number of RSUs granted covering an equal number of the Company's ordinary shares and the weighted-average grant date fair value of the RSUs granted:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
RSUs outstanding December 31, 2017	—	
Granted	36,924	$ 13.00
Shares vested	—	
Forfeited	—	
RSUs outstanding December 31, 2018	36,924	$ 13.00
Granted	31,367	$ 7.01
Shares vested	(36,924)	$ 13.00
Forfeited	—	
RSUs outstanding December 31, 2019	31,367	$ 7.01

The fair value of the RSUs is determined on the date of grant based on the market price of the Company's ordinary shares on that date. The fair value of RSUs is expensed ratably over the vesting period, which is generally one year for directors. Total expense recognized related to the RSUs was $313 and $289 for the years ended December 31, 2019 and 2018, respectively. Total unamortized compensation expenses related to the RSUs was $99 and $191 as of December 31, 2019 and December 31, 2018, respectively, expected to be recognized over a remaining average vesting period of 0.45 years and 0.40 years as of December 31, 2019 and December 31, 2018, respectively.

The Company awarded 50,000 RSUs to certain employees during the year ended December 31, 2019 which are subject to certain vesting conditions (Performance RSUs). No Performance RSUs were awarded prior to the year ended December 31, 2019.

The table below shows the number of Performance RSUs granted covering an equal number of the Company's ordinary shares and the weighted-average grant date fair value of the Performance RSUs granted:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Performance RSUs outstanding December 31, 2018	—	
Granted	50,000	$8.21
Shares vested	—	
Forfeited	—	
Performance RSUs outstanding December 31, 2019	50,000	$8.21

The weighted average grant date fair value of Performance RSUs with a market condition was determined using the Monte Carlo simulation model. The fair value of Performance RSUs is expensed ratably over the vesting period. Total expense recognized related to the Performance RSUs was $212 for the year ended December 31, 2019. Total unamortized compensation expenses related to Performance RSUs was $198 as of December 31, 2019 expected to be recognized over a remaining average vesting period of 0.81 years as of December 31, 2019.

The Company's share-based compensation expense was classified in the consolidated statements of operations and comprehensive loss as follows:

	Year ended December 31,		
	2019	2018	2017
Research and development expense	$ 723	$ 398	$ 139
General and administrative expense	1,450	892	253

There was a total of $3,639, $3,273 and $988 unamortized share-based compensation expense for restricted ordinary shares, options, restricted share units and performance restricted share units as of December 31, 2019, December 31, 2018 and December 31, 2017, respectively, expected to be recognized over a remaining average vesting period of 2.44 years, 2.71 years and 2.53 years as of December 31, 2019, December 31, 2018 and December 31, 2017, respectively.

(11) Income Taxes

During the years ended December 31, 2019, 2018 and 2017, the Company recorded no income tax benefits for the net operating losses incurred in each year due to its uncertainty of realizing a benefit from those items.

The provision for income taxes consists of the following components:

	Year ended December 31,		
	2019	2018	2017
Current			
U.S.	$ 444	$ 472	$ 444
Ireland	—	—	—
Total Current	$ 444	$ 472	$ 444
Deferred			
U.S.	$ —	$ —	$ —
Ireland	—	—	—
Total Deferred	$ —	$ —	$ —
Income Tax Provision	$ 444	$ 472	$ 444

Income taxes have been based on the following components of income (loss) before provision for income taxes:

	Year ended December 31,		
	2019	2018	2017
U.S.	$484	$532	$875
Ireland	(103,170)	(77,116)	(29,837)
Total	$(102,686)	$(76,584)	$(28,962)

The Irish federal statutory rate is reconciled to the effective tax rate as follows:

	Year ended December 31, 2019		Year ended December 31, 2018		Year ended December 31, 2017	
Statutory rate	12.50%	$(12,836)	12.50%	$(9,573)	12.50%	$(3,620)
Impact of U.S. tax rate	(0.07)%	72	(0.11)%	81	(0.80)%	232
Impact of valuation allowance	(12.91)%	13,258	(11.42)%	8,749	(13.64)%	3,949
Research and development tax credit	0.23%	(232)	0.45%	(341)	0.76%	(220)
Adjustments for current tax of prior periods	(0.24)%	241	0.00%	—	0.00%	—
Other, net	0.06%	(59)	(2.03)%	1,557	(0.36)%	103
Effective tax rate	(0.43)%	$444	(0.61)%	$472	(1.54)%	$444

The significant components of the Company's deferred tax assets and liabilities are as follows:

	Year ended December 31,		
	2019	2018	2017
Deferred tax assets			
Share-based compensation	$ 679	$ 27	$ 3
Depreciation	(24)	(49)	6
Net operating loss carryforwards	26,195	13,648	5,409
163(j) interest expense limitation	730	115	—
Other	84	665	239
Valuation allowance	(27,664)	(14,406)	(5,657)
Total deferred tax assets	$ —	$ —	$ —
Deferred tax liabilities			
	—	—	—
Total deferred tax assets	$ —	$ —	$ —
Net deferred tax asset	$ —	$ —	$ —

As a Company incorporated in Ireland, it is principally subject to taxation in Ireland.

The Company has net operating loss carryforwards in Ireland of approximately $26,195, $13,648 and $5,409 as of the years ended December 31, 2019, 2018 and 2017, respectively, for which a full valuation allowance has been recognized as it was determined that it is more-likely-than-not that these net deferred tax assets will not be realized. The net operating loss carryforwards do not expire, but are carried forward indefinitely. Realization of these deferred tax assets is dependent on the generation of sufficient taxable income. If the Company demonstrates consistent profitability in the future, the evaluation of the recoverability of these deferred tax assets may change and the remaining valuation allowance may be released in part or in whole. While management expects to realize the deferred tax assets, net of valuation allowances, changes in estimates of future taxable income or in tax laws may alter this expectation.

On December 22, 2017, the United States federal government enacted the Tax Act, marking a change from a worldwide tax system to a modified territorial tax system in the United States. As part of this change, the Tax Act, among other changes, provided a reduction of the U.S. federal corporate income tax rate from 34% to 21%, an indefinite carryforward of net operating losses incurred in 2018 and future periods, and an interest limitation starting in 2018 with an indefinite carryforward. Any impact to the Company related to these items were accounted for in the 2017, 2018 and 2019 tax provisions with minimal impact.

A reconciliation of the beginning and ending amount of gross unrecognized tax benefits is as follows:

	2019	2018
Balance at January 1	$ 428	$ 30
Additions	2,033	398
Balance at December 31	$ 2,461	$ 428

The Company is generally subject to examination in the Company's primary tax jurisdictions for tax years beginning 2015. The Company is not currently subject to any audits or examination.

(12) Commitments and Contingencies

License Agreement

On November 18, 2015, the Company entered into a license agreement with Pfizer for the worldwide exclusive rights to research, develop, manufacture and commercialize sulopenem.

As part of the license agreement, the Company is obligated to pay Pfizer potential future regulatory milestone payments, as well as sales milestones upon achievement of net sales ranging from $250.0 million to $1.0 billion for each product type. The Company is

also obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage based on marginal net sales of each licensed product.

Payments to Supplier

In June 2016, the Company entered into an agreement with a supplier whereby the Company would pay $2,807 (€2,500) to the supplier to acquire equipment which will be used solely to manufacture product for the Company. In June 2018, the Company entered into a supplemental agreement with this supplier whereby the Company would pay an additional $2,301 (€2,050) under the same terms as the original agreement. These payments will be offset against the price of the product to be supplied under a future supply agreement. No balance remained outstanding to the supplier as of December 31, 2019. $1,604 remained outstanding to the supplier as of December 31, 2018.

Contingencies

Liabilities for loss contingencies arising from claims, assessments, litigation, fines, penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. At each reporting date the Company evaluates whether or not a potential loss amount or a potential loss range is probable and reasonably estimable under the provisions of the authoritative guidelines that address accounting for contingencies. The Company expenses costs as incurred in relation to such legal proceedings. The Company is not currently involved in any legal matters arising in the normal course of business.

Under the terms of their respective employment agreements, each of the executive officers is eligible to receive severance payments and benefits upon a termination without “cause” or due to “permanent disability”, or upon “resignation for good reason”, contingent upon the named executive officer’s continued performance for the Company.

(13) Debt

On April 27, 2018, the Company’s subsidiaries, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited (The Borrowers), entered into a Loan and Security Agreement with SVB pursuant to which SVB agreed to lend the Borrowers up to $30,000 in two term loans. $15,000 of the secured credit facility was funded on closing. A second draw of up to $15,000 was available to the Company through October 31, 2019, upon satisfaction of either of the following: (i) the achievement by the Company of both non-inferiority and superiority primary endpoints from its Phase 3 uncomplicated urinary tract infection (uUTI) trial, as well as reporting satisfactory safety data from the trial, or (ii) the achievement of non-inferiority primary endpoints from both its Phase 3 uUTI and complicated urinary tract infection (cUTI) trials, as well as reporting satisfactory safety data from the trials. A non-utilization fee of 1.50% of the aggregate undrawn principal amount was to apply if the Company satisfied the above conditions but chose not to draw down the second term loan. The Company did not satisfy the conditions for the second draw above before the deadline of October 31, 2019.

Required monthly amortization payments for the initial $15,000 draw commenced on November 1, 2019 and total principal repayments of $1,034 were made during the year ended December 31, 2019. Interest accrues at a floating per annum rate equal to the greater of (i) 8.31%; or (ii) 3.89% above the Wall Street Journal prime rate, and is payable monthly in arrears. All outstanding principal, plus a 4.20% final interest payment, will be due and payable on the earliest to occur of March 1, 2022 (the maturity date), the acceleration of the term loan or the prepayment of the term loan. The final payment fee of $630 which represents 4.2% of the funded loan, is accreted using the effective interest method over the life of the loan as interest expense. Voluntary prepayments are permitted at any time, subject to a prepayment fee of 4.00% in the first year, 3.00% in the second year, and 2.00% thereafter.

In connection with the initial $15,000 draw, the Company issued SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B convertible preferred shares (which converted into warrants to purchase 19,890 ordinary shares upon the Company’s IPO) at an exercise price of $18.85 per share. Had the second term loan been drawn down, each of SVB and LSF would have been automatically entitled to purchase additional ordinary shares in an aggregate amount equal to 2.50% of the second term loan divided by the applicable exercise price.

The loan proceeds were allocated based on the relative fair values of the debt instrument and the warrant instrument. The fair value of the warrants and the closing costs were recorded as debt discounts and are being amortized using the effective interest rate method over the term of the loan. The effective annual interest rate of the outstanding debt is approximately 11.28% as of December 31, 2019. The Company recognized $1,761 and $1,169 of interest expense related to the loan agreement during the years ended December 31, 2019 and 2018, respectively, including $362 and $360 related to the accretion of the debt discounts and deferred financing costs during the years ended December 31, 2019 and 2018, respectively.

Scheduled principal payments on outstanding debt, as of December 31, 2019, are as follows:

Year Ending December 31,	
2020	6,207
2021	6,207
2022	1,552
	$ 13,966

(14) Quarterly Financial Data (unaudited)

	Three months ended			
	December 31, 2019	September 30, 2019	June 30, 2019	March 31, 2019
Revenue	$ —	$ —	$ —	$ 37
Total operating expenses	(23,178)	(30,999)	(27,378)	(20,503)
Net loss and comprehensive loss	(23,641)	(31,271)	(27,638)	(20,580)
Net loss attributable to ordinary shareholders	(23,641)	(31,271)	(27,638)	(20,580)
Net loss per share attributable to ordinary shareholders – basic and diluted	$ (1.59)	$ (2.15)	$ (1.93)	$ (1.44)
Weighted average ordinary shares outstanding – basic and diluted	14,866,838	14,571,278	14,340,231	14,290,437

	Three months ended			
	December 31, 2018	September 30, 2018	June 30, 2018	March 31, 2018
Revenue	$ 239	$ 254	$ 185	$ 191
Total operating expenses	(24,183)	(25,240)	(15,611)	(12,394)
Net loss and comprehensive loss	(24,258)	(24,905)	(15,747)	(12,146)
Net loss attributable to ordinary shareholders	(24,258)	(24,905)	(15,747)	(12,146)
Net loss per share attributable to ordinary shareholders – basic and diluted	$ (1.72)	$ (1.77)	$ (2.22)	$ (61.36)
Weighted average ordinary shares outstanding – basic and diluted	14,108,604	14,034,631	7,085,655	197,949

(15) Subsequent Events

On January 21, 2020, the Company completed a private placement pursuant to which its wholly owned subsidiary, Iterum Bermuda issued and sold approximately $51.6 million aggregate principal amount of Exchangeable Notes and $0.1 million aggregate principal amount of RLNs to a group of accredited investors. The Securities were sold in Units with each Unit consisting of and Exchangeable Note in the original principal amount of $1,000 a nd 50 RLNs. The Units were sold at a price of $1,000 per Unit. The Exchangeable Notes are exchangeable for the Company's ordinary shares at an initial exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $1.00 per ordinary share), subject to specified limitations. The RLNs entitle holders to payments based on a percentage of the Company's net revenues from potential U.S. sales of specified sulopenem products, subject to the terms and conditions of the indenture governing the RLNs. Pursuant to the indenture governing the RLNs, the payments on the RLNs will be up to either 15% or 20% of net revenues from U.S. sales of such products, depending on the indication approved by the FDA. The aggregate amount of payments on each RLN is capped at $160.00 (or 4,000 times the principal amount of such RLN). Iterum Bermuda received net proceeds from the sale of the Securities of approximately $46.7 million, after deducting placement agent fees and estimated offering expenses.

The Units were issued by Iterum Bermuda, which was formed on November 6, 2019 and is a 100% owned "finance subsidiary" of the Company under Rule 3-10 of Regulation S-X with no independent function other than financing activities. Iterum Therapeutics plc, as the parent company, has no independent assets or operations, and its operations are conducted solely through its

subsidiaries. The Company and each of its subsidiaries other than Iterum Bermuda (the " Subsidiary Guarantors") have provided a full and unconditional guarantee of Iterum Bermuda's obligations under the Exchangeable Notes and the RLNs, and each of the guarantees constitutes the joint and several obligations of the applicable guarantor . The Subsidiary Guarantors are 100% directly or indirectly owned subsidiaries of the Company . There are no significant restrictions upon the Company's or the Subsidiary Guarantors' ability to obtain funds from their subsidiaries by dividend or loan. None of the assets of Iterum Bermuda or the Subsidiary Guarantors represent restricted net assets pursuant to Rule 4-08(e)(3) of Regulation S-X.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2019. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2019, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), we conducted an evaluation of the effectiveness of our internal control over financial reporting. We used the 2013 framework in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission to evaluate the effectiveness of our internal control over financial reporting. Based on our evaluation under that framework, our management has concluded that our internal control over financial reporting was effective as of December 31, 2019.

Our independent registered public accounting firm has not performed an evaluation of our internal control over financial reporting during any period in accordance with the provisions of the Sarbanes-Oxley Act. For as long as we remain an ''emerging growth company'' as defined in Rule 12b-2 of the Exchange Act, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the year ended December 31, 2019, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Code of Ethics

We have adopted a written Code of Business Conduct and Ethics that applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The Code of Business Conduct and Ethics is available on our website at www.iterumtx.com. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website or in a Current Report on Form 8-K.

Directors

The following table sets forth information regarding our directors as of February 29, 2020:

Name	Age	Position
Corey N. Fishman	55	Director, Chief Executive Officer
Brenton K. Ahrens(2)	57	Director, Interim Chairman of the Board
Mark Chin(1)(2)	38	Director
Patrick J. Heron(3)	49	Director
Ronald M. Hunt(1)(3)	55	Director
David G. Kelly(2)(3)	59	Director
Shahzad Malik, M.D.(1)(3)	53	Director

(1) Member of the compensation committee
(2) Member of the audit committee
(3) Member of the nominating and corporate governance committee

Corey N. Fishman has served as our Chief Executive Officer and member of our board of directors since November 2015. From August 2010 to February 2015, Mr. Fishman served as chief operating officer of Durata Therapeutics, Inc., a pharmaceutical company acquired by Actavis plc, a pharmaceutical company, and he also served as chief financial officer of Durata Therapeutics, Inc., from June 2012 to February 2015. From 2008 to 2010, Mr. Fishman served as chief financial officer of GANIC Pharmaceuticals, Inc., a pharmaceutical company. From 2002 to 2008, Mr. Fishman served in a variety of roles at MedPointe Healthcare, Inc., a specialty pharmaceutical company acquired by Meda AB, including as chief financial officer from 2006 to 2008. Mr. Fishman currently serves as a member of the board of directors of Momenta Pharmaceuticals, Inc., a biotechnology company. Mr. Fishman holds a B.A. in economics from the University of Illinois at Urbana-Champaign and an M.S.M. in finance from the Krannert School of Management at Purdue University. We believe Mr. Fishman is qualified to serve on our board of directors due to his role as a founder of our Company, his deep knowledge of our Company and his extensive background in the pharmaceutical industry.

Brenton K. Ahrens has served as a member of our board of directors since November 2015. Since 1999, Mr. Ahrens has served as a general partner with Canaan Partners LLP, a venture capital firm. Prior to joining Canaan Partners, Mr. Ahrens worked in both commercial and technical roles at General Surgical Innovations, a biotechnology company, Ethicon (J&J), a medical device company, and IAP Research, an engineering company. Mr. Ahrens previously served on the board of directors of Durata Therapeutics, Inc., and continues to serve on a number of other private pharmaceutical and healthcare company boards. Mr. Ahrens holds a B.S. and an M.S. in mechanical engineering from the University of Dayton and an M.B.A. from the Tuck School of Business at Dartmouth College. We believe Mr. Ahrens is qualified to serve on our board of directors due to his investment experience, including service on the boards of directors of other healthcare companies.

Mark Chin has served as a member of our board of directors since May 2017. Since August 2016, Mr. Chin has served as an investment manager at Arix Bioscience plc, a life science investment company. From September 2012 to July 2016, Mr. Chin served as a principal at Longitude Capital LLC, a healthcare venture capital firm. From January 2011 to September 2012, Mr. Chin served as a consultant with the Boston Consulting Group. Mr. Chin currently serves on the board of Harpoon Therapeutics, Inc., a clinical-stage immunotherapy company. Mr. Chin has a B.S. in management science from the University of California at San Diego, an M.B.A. from the Wharton School at the University of Pennsylvania and an M.S. in biotechnology from the University of Pennsylvania. We believe Mr. Chin is qualified to serve on our board of directors due to his investment experience in biotechnology and medical technology industries.

Patrick J. Heron has served as a member of our board of directors since November 2015. Since 1999, Mr. Heron has served as a general partner with Frazier Healthcare Partners, a venture capital firm. Prior to joining Frazier Healthcare Partners, Mr. Heron worked at the management consulting firm McKinsey & Company. Before McKinsey, Mr. Heron held positions with Massachusetts General Hospital and biotechnology firm Cetus Corporation. Mr. Heron previously served on the boards of directors of pharmaceutical companies Tobira Therapeutics, Inc. , Cidara Therapeutics, Inc., Silvergate Pharmaceutical, Inc., Recida Therapeutics, Inc. and Collegium Pharmaceuticals, Inc. and continues to serve on the boards of directors of the following biotechnology companies: Imago BioSciences, Amunix Therapeutics, SutroVax, Inc., Arcutis Biotherapeutics , Inc., Scout Bio, Inc., Passage Bio,Inc. and Mirum Pharmaceuticals, Inc. Mr. Heron holds a B.A. in political science from the University of North Carolina at Chapel Hill and received an M.B.A. from Harvard Business School. We believe Mr. Heron is qualified to serve on our board of directors due to his extensive business experience, his experience in investing, and his experience in the life sciences industry.

Ronald M. Hunt has served as a member of our board of directors since November 2015. Since 2005, Mr. Hunt has served as a managing director and member of New Leaf Venture Partners, L.L.C., a venture capital firm. Previously, Mr. Hunt served at the Sprout Group, a venture capital firm and was a consultant with consulting firms Coopers & Lybrand Consulting and The Health Care Group. Mr. Hunt also previously served in various sales and marketing positions at Johnson & Johnson and SmithKline Beecham Pharmaceuticals. Mr. Hunt currently serves as a board member of Harpoon Therapeutics, Inc., a clinical-stage immunotherapy company and on the boards of a number of private pharmaceutical and healthcare companies. Mr. Hunt previously served on the board of directors of Neuronetics, Inc. Mr. Hunt holds a B.S. from Cornell University and an M.B.A. from the Wharton School of the University of Pennsylvania. We believe Mr. Hunt is qualified to serve on our board of directors due to his investment experience, his experience in the pharmaceuticals industry and his service on the boards of directors of other biopharmaceutical companies.

David G. Kelly has served as a member of our board of directors since August 2016. From September 2014 to January 2020 , Mr. Kelly served as the executive vice president, Ireland of Horizon Therapeutics , plc, a biopharmaceutical company. Mr. Kelly served as managing director, Ireland of Horizon Therapeutics, plc until July 2018. From February 2012 to September 2014, Mr. Kelly served as chief financial officer of Vidara Therapeutics Inc., a pharmaceutical company. From May 2005 to January 2012, Mr. Kelly served as chief financial officer of AGI Therapeutics plc, a pharmaceutical company. Mr. Kelly also served as senior vice president, finance and planning of Warner Chilcott plc (formerly Galen Holdings plc), a pharmaceutical company listed on the London Stock Exchange (LSE). In addition, Mr. Kelly held roles at Elan Corporation, a pharmaceutical company, and KPMG. Mr. Kelly holds a B.A. in economics from Trinity College, Dublin and is also a member of the Institute of Chartered Accountants in Ireland (ACA). We believe Mr. Kelly is qualified to serve on our board of directors due to his experience as a senior executive, particularly within the life science industry, including his experience in finance.

Shahzad Malik, M.D. has served as a member of our board of directors since May 2017. Since 1999, Dr. Malik has served as a general partner at Advent Life Sciences LLP, a venture capital firm. Prior to joining Advent, Dr. Malik spent six years practicing medicine before joining the London office of McKinsey & Company, a management consulting firm. Dr. Malik previously served on the boards of directors of Conatus Pharmaceuticals Inc., a pharmaceutical company, Agenus Inc., a biotechnology company, Aravive, Inc. (formerly Versartis, Inc.) , a biopharmaceutical company, and Axonics Modulation Technologies, Inc., a medical technology company. Dr. Malik continues to serve on the boards of directors of a number of other private pharmaceutical and healthcare company boards. Dr. Malik holds an M.A. from Oxford University and an M.D. from Cambridge University. He subsequently specialized in interventional cardiology while also pursuing research interests in heart muscle disorders both in the clinic and basic science laboratory. We believe Dr. Malik is qualified to serve on our board of directors due to his experience practicing medicine and his investment experience.

Executive Officers

The following table sets forth information regarding our executive officers as of February 29, 2020:

Name	Age	Position
Corey N. Fishman	55	Director, Chief Executive Officer
Michael W. Dunne	60	Chief Scientific Officer
Judith M. Matthews	50	Chief Financial Officer

In additon to the biographical information for Mr. Fishman, which is set forth above, set forth below is certain biographical information about Dr. Dunne and Ms. Matthews:

Michael W. Dunne, M.D. has served as our Chief Scientific Officer since November 2015. From November 2014 until September 2015, Dr. Dunne was vice president research and development at Actavis. From September 2010 to October 2014, Dr. Dunne served as chief medical officer of Durata Therapeutics, Inc., where he previously served as acting chief medical officer on a consulting basis from December 2009 to September 2010. From 1992 to 2009, Dr. Dunne served in a variety of roles in connection with the clinical development of numerous infectious disease compounds at Pfizer Inc., a biopharmaceutical company, including as the vice president, therapeutic head of development for infectious disease from 2001 to 2009. Dr. Dunne holds a B.A. in economics from Northwestern University and an M.D. from the State University of New York Health Sciences Center. He completed his internal medicine residency and fellowships in infectious diseases and pulmonary medicine at Yale University School of Medicine.

Judith M. Matthews has served as our Chief Financial Officer since November 2015. From 2012 to February 2015, Ms. Matthews served as vice president of finance at Durata Therapeutics, Inc. From 2009 to 2012, Ms. Matthews served as head of financial planning & analysis at Bally Total Fitness Corporation, a fitness club chain. From 2004 to 2008, Ms. Matthews served as vice president of finance for the Sterno Group, a subsidiary of Blyth, Inc., a home products company. Ms. Matthews holds a B.A. in accounting from the University of Illinois at Urbana-Champaign and a Master of Management in finance and marketing from the Kellogg School of Management at Northwestern University.

Audit Committee

Our audit committee consists of David G. Kelly (Chairman), Brenton K. Ahrens and Mark Chin. The chairperson of our audit committee is Mr. Kelly.

Our board of directors has determined that Messrs. Kelly, Ahrens and Chin each satisfy the independence standards for such committees established by the SEC and the Nasdaq Stock Market.

Our board of directors has determined that Mr. Kelly is an “audit committee financial expert” within the meaning of SEC regulations. Our board of directors has also determined that each member of our audit committee has the requisite financial expertise required under the applicable requirements of the Nasdaq Stock Market. In arriving at this determination, the board of directors has examined each audit committee member’s scope of experience and the nature of their employment in the corporate finance sector.

Director Designation Rights

Pursuant to the terms of an investor rights agreement (the 2020 Investor Rights Agreement) that we entered into in January 2020 with the purchasers in the January 2020 private placement pursuant to which our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited, sold units consisting of (i) 6.500% Exchangeable Senior Subordinated Notes due 2025 and (ii) Limited Recourse Royalty-Linked Subordinated Notes, for so long as Sarissa Capital Management LP (Sarissa) and its affiliates own at least 5% or 12.5%, as applicable, of our outstanding ordinary shares on a fully diluted basis, promptly, and in any event no more than 5 business days following written request of Sarissa, we will cause our board of directors to increase to consist of nine or 10 members, as applicable, and we will cause the board of directors to consist of no more than 10 members without the prior written consent of Sarissa. In addition, for so long as Sarissa and its affiliates own at least 12.5% of our outstanding ordinary shares on a fully diluted basis, Sarissa will have the right to designate two directors to our board of directors and, for so long as Sarissa and its affiliates own at least 5% but less than 12.5%, it will have the right to designate one director to our board of directors (Investor Designees). Pursuant to the terms of the 2020 Investor Rights Agreement, such Investor Designees will be appointed to our board of directors and to be members of the class of directors that was subject to reelection at our most recent annual meeting of shareholders. The Investor Designees will be entitled to be a member of any committee of our board of directors subject to the terms of the 2020 Investor Rights Agreement. Pursuant to the terms of the 2020 Investor Rights Agreement, the purchasers party thereto, subject to specified exceptions, have agree with us to vote in favor of the election of the Investor Designees, and we have agreed to cause the Investor Designees to be named in any relevant proxy statement.

Item 11. Executive Compensation.

The following discussion provides details of the compensation and other benefits paid by us and our subsidiaries to certain executive officers for services provided for the years ended December 31, 2019 and 2018 and to the members of our board of directors for services provided for the year ended December 31, 2019.

Executive and Director Compensation Processes

Our executive compensation program is administered by our compensation committee, subject to oversight by our board of directors. Our compensation committee reviews our executive compensation practices on an annual basis and approves, or recommends for approval by the board, thecompensation of the Company's executives.

Our compensation committee periodically reviews and makes recommendations to the board of directors with respect to director compensation.

For the years ended December 31, 2019 and 2018, at the direction of our compensation committee, our Company retained Frederic W. Cook & Co., Inc, or FW Cook, as an independent compensation consultant to provide comparative data on executive compensation practices in our industry and to provide advice to the compensation committee in relation to our executive compensation program generally, including advice and recommendations on the amounts and forms of executive compensation. While FW Cook provides advice to the company and the compensation committee in relation to such compensation practices, the compensation committee ultimately makes its own decisions with regard to our executive and director compensation programs.

The compensation committee reviewed information regarding the independence and potential conflicts of interest of FW Cook, taking into account, among other things (i) the provision of other services to the Company by FW Cook; (ii) the amount of fees received by FW Cook from the Company as a percentage of its total revenue; (iii) FW Cook's policies and procedures to prevent conflicts of interest; (iv) any business or personal relationships that FW Cook has with any member of the compensation committee; (v) any shares held by FW Cook in the Company; and (vi) any business or personal relationship FW Cook or FW Cook employees have with any executive officers of the Company. Based on this review, the compensation commitee concluded that the engagement did not raise any conflict of interest.

Executive Officer Summary Compensation Table

The following table provides details of the compensation and other benefits paid or accrued by us and our subsidiaries to our President and Chief Executive Officer and our two next most highly compensated executive officers, Mr. Michael W. Dunne M.D., our Chief Scientific Officer, and Ms. Judith M. Matthews, our Chief Financial Officer for services provided for the years ended December 31, 2019 and 2018:

Name and Principal Position	Year Ended December 31,	Salary ($)	Share Awards(1) ($)	Option Awards(1) ($)	Non-Equity Incentive Plan Compensation(2) ($)	All Other Compensation(3) ($)	Total ($)
Corey N. Fishman	2019	551,138	123,150	561,000	151,841	4,902	1,392,031
President and Chief Executive Officer	2018	494,546	—	953,529	305,910	2,622	1,756,607
Michael W. Dunne, M.D.	2019	402,794	73,890	317,900	81,000	7,524	883,108
Chief Scientific Officer	2018	377,606	—	595,957	166,551	4,902	1,145,016
Judith M. Matthews	2019	356,417	32,840	112,200	62,475	1,161	565,093
Chief Financial Officer	2018	305,707	—	178,786	126,175	995	611,663

(1) The amounts reported do not reflect the amounts actually received by our executive officers. Instead, these amounts reflect the aggregate grant date fair values of performance restricted share units and share options granted to our executive officers during the years ended December 31, 2019 and 2018, respectively, as computed in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, 718. Assumptions used in the calculation of these amounts are included in Note 10 to our audited financial statements included in this 10-K. As required by SEC rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions. Our executive officers who have received options will only realize compensation with regard to these options to the extent the trading price of our ordinary shares is greater than the exercise price of such options.
(2) Amount represents cash bonuses earned for the 12-month periods ending December 31, 2019 and 2018, respectively. Amounts disclosed for the year ended December 31, 2019 exclude payments made in 2019 for 2018 bonuses. Amounts disclosed for the year ended December 31, 2018 exclude payments made in 2018 for 2017 bonuses.
(3) Includes the dollar value of life insurance premiums paid by the company for the benefit of such executive.

Narrative Disclosure to Executive Officer Summary Compensation Table

Base Salary

During the year ended December 31, 2019, we paid base salaries of $551,138 to Mr. Fishman, $402,794 to Dr. Dunne and $356,417 to Ms. Matthews. During the year ended December 31, 2018, we paid base salaries of $494,546 to Mr. Fishman, $377,606 to Dr. Dunne and $305,707 to Ms. Matthews.

In February 2020, our compensation committee approved, consistent with the recommendations of the compensation committee's independent compensation consultant who, in 2020, was CODA Advisors, LLC, an increase to the base salaries of Mr.

Fishman, Dr. Dunne and Ms. Matthews as follows: $561,813 for Mr. Fishman, $412,088 for Dr. Dunne and $363,248 for Ms. Matthews.

None of the named executive officers are currently party to any employment arrangements that provide for automatic or scheduled increases in base salary.

Non-Equity Incentive Plan Compensation

Our named executive officers participate in a cash bonus program which is tied to the achievement of strategic and corporate goals of the Company, which are approved annually by our compensation committee. Our compensation committee determines the amount of these bonuses, if any, based on its assessment of the named executive officers' performance and that of the Company against goals established annually.

Under their respective employment agreements, the annual target bonus for Mr. Fishman is 55% of his current base salary, the annual target bonus for Dr. Dunne is 40% of his current base salary and the annual target bonus for Ms. Matthews is 35% of her current base salary.

At the beginning of each year, our compensation committee reviews the accomplishments of the named executive officers as measured against the the previous year's goals, whether each goal had been achieved and the relative weight that should be given to each goal in determining the cash bonus payment for that year. Based on its review, the compensation committee recommended cash bonus payments of $151,841 to Mr. Fishman, $81,000 to Dr. Dunne and $62,475 to Ms. Matthews with respect to the year ended December 31, 2019. The compensation committee recommended cash bonus payments of $305,910 to Mr. Fishman, $166,551 to Dr. Dunne and $126,175 to Ms. Matthews with respect to the year ended December 31, 2018.

Equity Incentive Awards

We believe that our ability to grant equity-based awards is a valuable and necessary compensation tool that aligns the long-term financial interests of our executive officers and our shareholders. In addition, we believe that our ability to grant options and other equity-based awards helps us to attract, retain and motivate our executive officers and encourages them to devote their best efforts to our business and financial success.

In February 2020, pursuant to powers delegated to it by the board of directors, our compensation committee approved the grant of performance restricted stock units, or PSUs, under our 2018 Equity Incentive Plan to our named executive officers which are subject to certain performance based vesting conditions. The following number of PSUs were granted to the executive officers: 335,000 to Mr. Fishman, 160,000 to Dr. Dunne and 125,000 to Ms. Matthews. These PSUs shall vest in the following proportions: (i) 50% upon Board certification of the acceptance by the United States Food and Drug Administration, or the FDA, of a New Drug Application, or NDA,, provided such event occurs on or before December 31, 2021; and (ii) 50% on the date which is the initial deadline set by the FDA to complete its review of such NDA in accordance with the Prescription Drug User Fee Act, provided such event occurs on or before December 31, 2021 and in each case such executive remains in continued service with us.

In January 2019, our compensation committee approved the grant of share options under the 2018 Equity Incentive Plan to the named executive officers to purchase the following number of shares, effective on February 15, 2019 : 150,000 to Mr. Fishman, 85,000 to Dr. Dunne and 30,000 to Ms. Matthews.25% of each option vested on February 15, 2020 based on each named executive officer's continued service with us through that date and the remaining 75% is scheduled to vest in equal monthly installments thereafter until February 15, 2023 subject to each named executive officer's continued provision of services to us on each vesting date. Each of the option awards has an exercise price of $5.80 per share, being the closing price on the Nasdaq Global Market on the date of grant.

In January 2019, the compensation committee also approved the grant of performance restricted stock units, or PSUs, under our 2018 Equity Incentive Plan to our named executive officers effective on February 15, 2019 and which are subject to certain performance based vesting conditions. The following number of PSUs were granted to the executive officers: 15,000 to Mr. Fishman, 9,000 to Dr. Dunne and 4,000 to Ms. Matthews. The vesting of these PSUs is subject to approval of an NDA of ours by the FDA and achievement of our ordinary shares on the Nasdaq Global Market of an average closing price that equals or exceeds $13 over any 20 consecutive trading days (from the period beginning 19 days prior to receipt of NDA approval) at a point in time when the executive remains in continued service with us and provided such events occur on or before December 31, 2021.

In March 201 8, the board of directors approved the grant of stock options under the 2018 Equity Incentive Plan to the named executive officers to purchase the following number of shares, effective on our initial public offering: 127,307 to Mr. Fishman, 79,567 to Dr. Dunne and 23,870 to Ms. Matthews. 25% of the options vested on May 24, 2019 with the remaining 75% scheduled to vest in equal monthly installments thereafter until May 24, 2022 subject to each named executive officer's continued provision of services to

us on each vesting date. Each of the option awards has an exercise price of $13.00 per share, being the closing price on the Nasdaq Global Market on the date of grant.

Outstanding Equity Awards at December 31, 2019

The following table presents information regarding outstanding equity awards held by our named executive officers as of December 31, 2019. All equity awards were granted under our 2015 Equity Incentive Plan and our 2018 Equity Incentive Plan.

	Option Awards				Share Awards	
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable(1)	Option Exercise Price Per Share(2)	Option Expiration Date	Equity incentive plan awards: Number of unearned shares, units or other rights that have not vested(3) (#)	Equity incentive plan awards: Market or payout value of unearned shares, units or other rights that have not vested ($)
Corey N. Fishman	36,759	28,592(4)	$3.30	09/11/2027	—	—
	50,392	76,915(5)	13.00	05/23/2028	—	—
	—	150,000(6)	5.80	02/14/2029	—	—
	—	—	—	12/31/2021	15,000	67,500
Michael W. Dunne, M.D.	23,392	18,195 (4)	3.30	09/11/2027	—	—
	31,495	48,072 (5)	13.00	05/23/2028	—	—
	—	85,000 (6)	5.80	02/14/2029	—	—
	—	—	—	12/31/2021	9,000	40,500
Judith M. Matthews	6,683	5,199 (4)	3.30	09/11/2027	—	—
	9,448	14,422 (5)	13.00	05/23/2028	—	—
	—	30,000 (6)	5.80	02/14/2029	—	—
	—	—	—	12/31/2021	4,000	18,000

(1) Pursuant to the equity agreements between the named executive officer and us, the vesting of such named executive officer's share and option awards will accelerate under certain circumstances as described under the section titled "—Potential Payments Upon Termination or Change in Control

(2) The exercise price per share of the stock options reflects the fair market value per ordinary share on the date of grant.

(3) The awards reported are performance restricted share units for which vesting is subject to approval of an NDA of ours by the FDA and achievement of our ordinary shares on the Nasdaq Global Market of an average closing price that equals or exceeds $13 over any 20 consecutive trading days (from the period beginning 19 days prior to receipt of NDA approval) at a point in time when the executive remains in continued service with us and provided that each such event occurs on or before December 31, 2021.

(4) Stock option that vested as to 1/4th of the shares underlying the option on September 12, 2018 with the remaining shares scheduled to vesting in equal monthly installments thereafter until September 12, 2021, subject to continued service with us through each relevant vesting date.

(5) Stock option that vested as to 1/4th of the shares underlying the option on May 24, 2019 with the remaining shares scheduled to vesting in equal monthly installments thereafter until May 24, 2022, subject to continued service with us through each relevant vesting date.

(6) Stock option that vested as to 1/4th of the shares underlying the option on February 15, 2020 with the remaining shares scheduled to vesting in equal monthly installments thereafter until February 15, 2023, subject to continued service with us through each relevant vesting date.

Employment Agreements with Executive Officers

We have entered into offer letters with each of our named executive officers. The offer letters generally provide for at-will employment and set forth the executive's initial base salary, target variable compensation, eligibility for employee benefits, the terms of initial equity grants and in some cases severance benefits on a qualifying termination. Each of our named executive officers has also executed our standard form proprietary information agreement. Any potential payment and benefits due upon a termination of employment or change of control of us are further described below.

Corey N. Fishman serves as our President and Chief Executive Officer. On November 18, 2015, Mr. Fishman entered into an offer letter with Iterum Therapeutics US Limited, our indirect wholly owned subsidiary. The offer letter has no specific term and constitutes an at-will employment arrangement. In 2017, Mr. Fishman's base salary was $420,000. On May 2, 2018, Mr. Fishman entered into an amended offer letter, which became effective upon the closing of our initial public offering pursuant to which Mr. Fishman's base salary became $540,000, and his discretionary annual target performance bonus increased from 50% to 55% of his annual base salary. His base salary was reviewed in January 2019 and increased to $552,150, effective February 1, 2019. His base salary was reviewed in February 2020 and increased to $561,813, effective February 1, 2020.

Michael W. Dunne, M.D. serves as our Chief Scientific Officer. On November 18, 2015, Dr. Dunne entered into an offer letter with Iterum Therapeutics US Limited, our indirect wholly owned subsidiary. The offer letter has no specific term and constitutes an at-will employment arrangement. Dr. Dunne's base salary pursuant to the offer letter was $350,000 and his discretionary annual target performance bonus is 40% of his annual base salary. In 2017, Dr. Dunne's base salary was $367,500 and in 2018 was $378,525. Dr.

Dunne's base salary was reviewed in January 2019 and was increased to $405,000, effective February 1, 2019. His base salary was reviewed in February 2020 and increased to $412,088, effective February 1, 2020.

Judith M. Matthews serves as our Chief Financial Officer. On November 18, 2015, Ms. Matthews entered into an offer letter with Iterum Therapeutics US Limited, our indirect wholly owned subsidiary. The offer letter has no specific term and constitutes an at-will employment arrangement. In 2017, Ms. Matthew's base salary was $236,250. Ms. Matthews entered into an amended offer letter, which became effective upon the closing of our initial public offering pursuant to which Ms. Matthews' base salary became $350,000, and her discretionary annual target performance bonus increased from 25% to 35% of her annual base salary. Ms. Matthew's base salary was reviewed in January 2019 and increased to $357,000, effective February 1, 2019. Her base salary was reviewed in February 2020 and increased to $363,248, effective February 1, 2020.

Potential Payments Upon Termination or Change in Control

Our agreements with each of our named executive officers provide that upon the termination of his or her employment by us other than for cause, or by the named executive officer with good reason (each as defined in the offer letters), he or she will be entitled to receive the following severance benefits:

- cash severance equal to a fixed number of months of such executive's base salary (twelve months in the case of Mr. Fishman and nine months in the case of Dr. Dunne and Ms. Matthews); and
- Company-paid COBRA premiums for up to 12 months following such executive's termination date.

If such a qualifying termination occurs within the period beginning one month prior to and ending 12 months following a change of control of us, the cash severance payment entitlement described above will increase to twelve months of such executive's then current base salary in the case of Dr. Dunne and Ms. Matthews, and to eighteen months of his then current base salary in the case of Mr. Fishman. The executives will also be entitled to an additional cash payment equal to a percentage of such executives' target annual bonus for the year of termination, equal to 100% in the case of Dr. Dunne and Ms. Matthews and 150% in the case of Mr. Fishman. In addition, each of Mr. Fishman, Dr. Dunne and Ms. Matthews' currently outstanding share awards will accelerate in full.

Each offer letter also contains a "better after-tax" provision, which provides that if any of the payments to such named executive officer constitutes a parachute payment under Section 280G of the Internal Revenue Code of 1986, as amended, or the Code, the payments will either be (i) reduced or (ii) provided in full to the executive, whichever results in the executive receiving the greater amount after taking into consideration the payment of all taxes, including the excise tax under Section 4999 of the Code, in each case based upon the highest marginal rate for the applicable tax.

Payment of any of the severance benefits described above is also conditioned on the named executive officer's delivery and non-revocation of a general release of claims in our favor.

On March 11, 2020, on recommendation from the compensation committee, our board of directors approved the creation of a carve out plan to reward certain key employees including Mr. Fishman, Dr. Dunne and Ms. Matthews in the event of a change of control. The aggregate amount payable under the plan will be calculated on a tiered basis based on the upfront consideration payable to us and our equityholders in connection with such change of control, with potential aggregate amounts payable under the plan falling within a range around approximately 2.5% of the upfront consideration. The other terms of the plan and each executive's entitlement to participate are to be determined at the time of the change of control transaction.

Director Compensation – Summary Compensation Table

The following table shows the total compensation paid or accruedby us and our subsidiaries during the year ended December 31, 2019 to each of our current and former non-employee directors. Directors who are employed by us are not compensated for their service on our board of directors.

Name	Fees Earned or Paid in Cash ($)	Share Awards(1)(2) ($)	Option Awards (1)(3) ($)	Other Compensation(6) ($)	Total ($)
Brenton K. Ahrens	42,500	—	80,000	—	122,500
Mark Chin	48,500	40,000	—	40,000	128,500
Paul R. Edick(4)	38,250	—	—	—	38,250
James I. Healy M.D., Ph.D.(5)	41,000	40,000	-	40,000	121,000
Patrick J. Heron	39,000	20,000	40,000	20,000	119,000
Ronald M. Hunt	51,000	40,000	—	40,000	131,000
David G. Kelly	59,000	80,000	—	—	139,000
Shahzad Malik, M.D.	45,000	—	80,000	—	125,000

(1) The amounts reported do not reflect the amounts actually received by our director. Instead, these amounts reflect the aggregate grant date fair values of restricted share units and stock options granted to our directors during the years ended December 31, 2019, as computed in accordance with FASB ASC 718. Assumptions used in the calculation of these amounts are included in Note 10 to our audited financial statements included in this 10-K. As required by SEC rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions. Our directors who have received options will only realize compensation with regard to these options to the extent the trading price of our ordinary shares is greater than the exercise price of such options.

(2) The aggregate number of outstanding restricted share units held by each of our non-employee directors as of December 31, 2019 were as follows: Mr. Ahrens: 0; Mr. Chin: 5,703; Mr. Edick: 0; Dr. Healy: 5,703; Mr. Heron: 2,852; Mr. Hunt: 5,703; Mr. Kelly: 11,406; and Dr. Malik: 0.

(3) The aggregate number of shares subject to outstanding share options units held by each of our non-employee directors as of December 31, 2019 were as follows: Mr. Ahrens: 19,671; Mr. Chin: 0; Mr. Edick: 0; Dr. Healy: 0; Mr. Heron: 9,836; Mr. Hunt: 11,241; Mr. Kelly: 3,182; and Dr. Malik: 30,912.

(4) Mr. Edick did not stand for reelection to our board of directors at our 2019 Annual General Meeting of Shareholders held on June 13, 2019 and his service as a director ceased on the date of such meeting.

(5) Dr. Healy resigned as a member of our board of directors on February 12, 2020.

(6) With respect to the portion of equity compensation to be made in restricted stock units, directors can elect for the award to be made in the form of a mixture of 50% cash and 50% shares on vesting. Other compensation represents that portion of the restricted stock units elected to be made in the form of cash.

On the expiry of Paul R. Edick's term of office as director on June 13, 2019, pursuant to an ordinary share subscription deed dated as of October 14, 2015 between us and Mr. Edick, the compensation committee approved the acceleration of all remaining unvested ordinary shares issued thereunder, being 331 ordinary shares. As a result, those ordinary shares were no longer subject to a right of repurchase by us. In addition, the compensation committee approved the acceleration of 1,060 options over ordinary shares held by Mr. Edick at a price of $3.30 such that on the expiry of his term as director, those share options became exercisable in full.

Non-Employee Director Compensation Policy

Under our Non-Employee Director Compensation Policy each non-employee director is eligible to receive compensation for his or her service consisting of annual cash retainers and equity awards. Each director receives an annual base cash retainer of $35,000 for such service, to be paid quarterly. The non-executive chairperson of our board of directors receives an additional annual base cash retainer of $27,500 for such service, to be paid quarterly.

The policy also provides that we compensate the members of our board of directors for service on our committees as follows:

- The chairperson of our audit committee receives an annual cash retainer of $15,000 for such service, paid quarterly, and each of the other members of the audit committee receives an annual cash retainer of $7,500, paid quarterly.
- The chairperson of our compensation committee receives an annual cash retainer of $12,000 for such service, paid quarterly, and each of the other members of the compensation committee receives an annual cash retainer of $6,000, paid quarterly.
- The chairperson of our nominating and corporate governance committee receives an annual cash retainer of $8,000 for such service, paid quarterly, and each of the other members of the nominating and corporate governance committee receives an annual cash retainer of $4,000, paid quarterly.

The policy further provides for the grant of annual equity awards as follows:

- Each director will receive annual equity awards with a fixed value of $80,000.
- The equity awards will be granted as a mix of share options and restricted stock units, at such director's discretion. Each director must determine their mix of equity awards no later than 30 days prior to the applicable grant date.
- All equity awards will vest on the one-year anniversary of the grant date.
- The value of a share option to be granted under this policy will be determined using the same method we use to calculate the grant-date fair value of share options in our financial statements, except that no provision will be made for estimated forfeitures related to service-based vesting. The actual number of shares to be granted under a restricted stock unit award under this policy will be determined by dividing the grant date value by a 30-day volume weighted average trading price (ending on the trading day immediately preceding the grant date).

We also reimburse our non-employee directors for reasonable travel and other expenses incurred in connection with attending our board of director and committee meetings.

For 2020, it was agreed that the right to receive an annual equity award would be waived by each of the non-executive directors with the exception of Mr. Kelly.

Risk Considerations in Our Compensation Program

Our compensation committee has reviewed and evaluated the philosophy and standards on which our compensation plans have been developed and implemented across our Company. It is our belief that our compensation programs do not encourage inappropriate actions or risk taking by our executive officers. We do not believe that any risks arising from our employee compensation policies and practices are reasonably likely to have a material adverse effect on our Company. In addition, we do not believe that the mix and design of the components of our executive compensation program encourage management to assume excessive risks.

2018 Equity Incentive Plan

Our board of directors adopted o ur 2018 Equity Incentive Plan, or the 2018 Plan, in March 2018 and our shareholders approved the 2018 Plan in May 2018.

Authorized Awards. Our 2018 Plan authorizes the award of incentive stock options that may qualify for favorable tax treatment under U.S. tax laws to their recipients under Section 422 of the Code, or ISOs, nonstatutory stock options, or NSOs, stock appreciation rights, or SARs, restricted stock, restricted stock units, or RSUs, performance-based awards, and other stock awards, which are collectively referred to as awards. We may grant awards under the 2018 Plan to our employees, including our officers, and employees of our affiliates. A separate sub-plan to the 2018 Plan has been established for the purpose of granting awards to our non-employee directors and consultants and non-employee directors and consultants of our affiliates, which we refer to as the Sub-Plan. The provisions of the 2018 Plan apply in their entirety to any awards made under the Sub-Plan save for certain amendments set out in the Sub-Plan required in the context of awards to non-employee directors and consultants and non-employee directors and consultants of our affiliates, rather than employees, including references to eligible participants under the Sub-Plan.

Share Reserve. Initially, the aggregate number of our ordinary shares that may be issued pursuant to awards under our 2018 Plan was 1,018,459 shares, which includes any shares subject to outstanding options or other awards that were granted under our 2015 Plan and that are forfeited, terminated, expire or are otherwise not issued. Additionally, upon board or committee approval the number of ordinary shares reserved for issuance under our 2018 Plan will increase on January 1 of each calendar year for ten years, starting on January 1, 2019 and ending on and including January 1, 2028, in an amount up to 4% of the total number of our ordinary shares outstanding on December 31 of the prior calendar year, or a lesser number of shares determined by our board of directors. On
December 5, 2018, pursuant to powers delegated to it by our board of directors, the compensation committee approved effective
January 1, 2019 an increase in the number of ordinary shares available to be granted pursuant to the 2018 Plan by 4% of the total number of issued share capital on December 31, 2018, being 574,081 ordinary shares. In February 2020, the compensation committee approved an increase in the number of ordinary shares available to be granted pursuant to the 2018 Plan by 594,758. As of December 31, 2019, options to purchase 936,618 ordinary shares were outstanding under our 2018 Plan, with a weighted-average exercise price of $8.97 per share. As of December 31, 2019, there were 31,367 and 50,000 ordinary shares to be issued upon vesting of outstanding RSUs and PSUs, respectively.

The maximum number of our ordinary shares that may be issued upon the exercise of ISOs under our 2018 Plan is equal to 3,055,377.

Shares subject to awards granted under our 2018 Plan that expire or terminate without being exercised in full, or that are paid out in cash rather than in shares, do not reduce the number of shares available for issuance under our 2018 Plan. Additionally, shares become available for future grant under our 2018 Plan if they were issued under awards under our 2018 Plan if we repurchase them or they are forfeited. This includes shares used to pay the exercise price of an award or to satisfy the tax withholding obligations related to an award.

Plan Administration. Our 2018 Plan is administered by our compensation committee, or by our board of directors or another duly authorized committee of our board of directors, acting in place of our compensation committee. Our board of directors or our compensation committee may also delegate to one or more of our officers the authority to designate employees (other than officers) to receive specified share awards, and determine the number of shares subject to such awards.

Our compensation committee has the authority to construe and interpret our 2018 Plan, grant and amend awards, determine the terms of such awards and make all other determinations necessary or advisable for the administration of the plan, including, but not limited to, repricing options or SARs without prior shareholder approval. Awards granted under the 2018 Plan may vest over time based on the holder's continued service with us, or following the achievement of certain pre-established performance goals.

Options. Options represent the right to purchase our ordinary shares on the date of exercise at a stated exercise price. ISOs may only be granted to employees of the Company and its subsidiaries. The exercise price of an option generally must be at least equal to the fair market value of our ordinary shares on the date of grant. Our compensation committee may provide for options to be exercised only as they vest or to be immediately exercisable with any shares issued on exercise being subject to our right of repurchase that lapses as the shares vest. The maximum term of options granted under our 2018 Plan is ten years.

Restricted Stock Awards. Restricted stock awards represent an offer by us to issue or sell our ordinary shares subject to vesting restrictions, which may lapse based on time or achievement of performance conditions. The price (if any) of a restricted stock award will be determined by our compensation committee. Unless otherwise determined by our compensation committee at the time of grant, vesting will cease on the date the participant no longer provides services to us and unvested shares will be forfeited.

Restricted Stock Unit Awards (RSUs) and Performance Restricted Stock Units (PSUs). RSUs and PSUs represent the right to receive our ordinary shares at a specified date in the future, subject to forfeiture of that right because of termination of employment or failure to achieve certain performance conditions. If an RSU/PSU award has not been forfeited, then on the date specified in the RSU/PSU agreement, we will deliver to the holder a number of whole ordinary shares, cash or a combination of our ordinary shares and cash. Additionally, dividend equivalents may be credited in respect of shares covered by an RSU/PSU award.

Stock Appreciation Rights. SARs provide for a payment, or payments, in cash or ordinary shares, to the holder based upon the difference between the fair market value of our ordinary shares on the date of exercise and the stated exercise price. The maximum term of SARs granted under our 2018 Plan is ten years.

Other Stock Awards. Our compensation committee may grant other awards based in whole or in part by reference to our ordinary shares. Our compensation committee will determine the number of shares under such award and all other terms and conditions of such awards.

Transferability. Awards granted under our 2018 Plan may not be transferred in any manner other than by will or by the laws of descent and distribution or as otherwise determined by our compensation committee or under the terms of our 2018 Plan or an applicable award agreement.

Changes to Capital Structure. In the event that there is a specified type of change in our capital structure, such as a share split or recapitalization, appropriate adjustments will be made to (i) the class and the maximum number of shares reserved for issuance under our 2018 Plan, (ii) the class and the maximum number of shares by which the share reserve may increase automatically each year, (iii) the class and the maximum number of shares that may be issued upon the exercise of ISOs, and (iv) the class and the number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding awards.

Corporate Transactions. Our 2018 Plan provides that in the event of certain specified significant corporate transactions, each outstanding award will be treated as determined by our board of directors unless otherwise provided in an award agreement or other written agreement between us and the award holder. The board of directors may take one of the following actions with respect to such awards:

- arrange for the assumption, continuation or substitution of an award by a successor corporation;
- arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation;

- accelerate the vesting, in whole or in part, of the award and provide for its termination prior to the transaction;
- arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us;
- cancel or arrange for the cancellation of the award, to the extent not vested or not exercised prior to the closing of the transaction, in exchange for a cash payment or no payment, as determined by our board of directors; and
- cancel or arrange for the cancellation of the award to the extent not vested but not exercised prior to the closing of the transaction, in exchange for a payment, in the form determined by our board of directors, equal to the excess, if any, of (A) the per share amount payable to holders of our ordinary shares in the transaction over (B) any exercise price payable by the participant in connection with the award, multiplied by the number of shares subject to the award.

- A corporate transaction generally will be deemed to occur in the event of: (i) a sale of all or substantially all of our assets, (ii) the sale or disposition of more than 50% of our outstanding securities, (iii) the consummation of a merger or consolidation where we do not survive the transaction and (iv) the consummation of a merger or consolidation where we do survive the transaction but our ordinary shares outstanding prior to such transaction are converted or exchanged into other property by virtue of the transaction. In addition, any one or more of the above events may be effected pursuant to (x) a takeover under Irish takeover rules; (y) a compromise or arrangement under Chapter 1 of Part 9 of the Irish Companies Act 2014 (Irish Companies Act) or (z) Chapter 2 of Part 9 of the Irish Companies Act.

- The board of directors is not obligated to treat all awards or portions of stock awards, even those that are of the same type, in the same manner.

- *Amendment and Termination.* Our board of directors or another duly authorized committee has the authority to amend, suspend, or terminate our 2018 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our shareholders. No ISOs may be granted after the tenth anniversary of the date our board of directors adopted our 2018 Plan, and no awards may be granted under our 2018 Plan while it is suspended or after it is terminated.

2015 Equity Incentive Plan

- Our board of directors adopted and our shareholders approved our 2015 Equity Incentive Plan, or the 2015 Plan, in November 2015. The 2015 Plan was amended most recently in May 2017. The 2015 Plan provides for the grant of ISOs, NSOs, restricted stock awards, RSUs, SARs, and other stock awards to our employees, directors and consultants.

- Since the 2018 Plan became effective, we no longer grant awards under the 2015 Plan. However, any outstanding awards granted under the 2015 Plan remain outstanding, subject to the terms of the 2015 Plan and stock option agreements, until such outstanding options are exercised or until they terminate or expire by their terms.

- *Authorized Shares.* As of December 31, 2019, options to purchase 213,652 ordinary shares were outstanding under our 2015 Plan, with a weighted-average exercise price of $3.31 per share. As of December 31, 2018, options to purchase 233,607 ordinary shares were outstanding under our 2015 Plan, with a weighted-average exercise price of $3.32 per share. The maximum number of ordinary shares that may be issued on the exercise of ISO under our 2015 Plan is the share reserve.

- *Plan Administration*. Our 2015 Plan may be administered by our board of directors or another duly authorized committee. Our 2015 Plan is currently administered by our compensation committee. Our board of directors or another duly authorized committee has the authority to construe and interpret our 2015 Plan, amend the plan and outstanding awards and make all other determinations necessary or advisable for the administration of the plan, including, but not limited to, repricing options or SARs without prior shareholder approval.

- *Corporate Transactions*. Our 2015 Plan provides that in the event of a corporate transaction, each outstanding award will be treated as determined by our board of directors unless otherwise provided in an award agreement or other written agreement between us and the award holder. The board of directors may generally take the same actions as summarized above in connection with awards under the 2018 Plan, and the definition of a corporate transaction under the 2015 Plan is substantially the same as such defined term in the 2018 Plan.

- *Transferability*. Awards granted under our 2015 Plan may not be transferred in any manner other than by will or by the laws of descent and distribution or as otherwise determined by our compensation committee or under the terms of our 2015 Plan or an applicable award agreement.

- *Plan Amendment or Termination*. Our board of directors or another duly authorized committee has the authority to amend, suspend, or terminate our 2015 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our shareholders.

Health and Welfare Benefits

All of our named executive officers are eligible to participate in our employee benefit plans, including our medical, dental, and vision insurance plans, in each case on the same basis as all of our other full-time employees.

***401(k)* Plan**

We maintain a defined contribution retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees may defer eligible compensation on a pre-tax basis, up to the statutorily prescribed annual limits on contributions under the Code. The Company is required to contribute a deferral rate of up to 3% to the 401(k) plan on behalf of certain employees. We have not historically made discretionary contributions to the 401(k) plan for the benefit of employees. Employee contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participant's directions. Employees are immediately and fully vested in their contributions. The 401(k) plan is intended to be qualified under Section 401(a) of the Code with the 401(k) plan's related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan.

Limitation on Liability and Indemnification of Directors and Officers

Our articles of association, and indemnification agreements with our board of directors and executive officers provide for indemnification for our directors and officers.

Rule 10b5-1* Sales *Plans

Our directors and officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell ordinary shares on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer generally may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may generally buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information, subject to compliance with the terms of our insider trading policy.

Compensation Committee Interlocks and Insider Participation

During 2019, the members of our compensation committee were Ronald M. Hunt (Chairman), Mark Chin, Paul R. Edick (to June 2019), James I. Healy, M.D., Ph.D., and Shahzad Malik, M.D. No member of our compensation committee is, or has ever been, an officer or employee of our Company. None of our executive officers serve, or have served during the last year, as a member of the board of directors, compensation committee, or other board committee performing equivalent functions of any other entity that has one or more executive officers serving as one of our directors or on our compensation committee.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters.

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of February 29, 2020 by:

(a) each person, or group of affiliated persons, known by us to beneficially own more than 5% of our ordinary shares;

(b) each of our named executive officers;

(c) each of our directors; and

(d) all of our executive officers and directors as a group.

Beneficial ownership is determined according to the rules of the SEC and generally means that a person has beneficial ownership of a security if he, she, or it possesses sole or shared voting or investment power of that security, including share options that are exercisable within 60 days of February 29, 2020. Our ordinary shares issuable pursuant to share options are deemed outstanding for computing the percentage of the person holding such options and the percentage of any group of which the person is a member but are not deemed outstanding for computing the percentage of any other person. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons named in the table below have sole voting and investment power with respect to all ordinary shares shown that they beneficially own, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Section 13(d) and 13(g) of the Securities Act of 1933, as amended. Percentage ownership is based on 15,772,360 ordinary shares outstanding on February 29, 2020. Except as otherwise set forth below, the address of the beneficial owner is c/o Iterum Therapeutics plc, Block 2 Floor 3 Harcourt Centre, Harcourt Street, Dublin 2, Ireland.

	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
Principal Shareholders		
Entities affiliated with Advent Life Sciences[1]	868,161	5.8%
Entities affiliated with Arix Bioscience[2]	1,089,903	7.3%
Entities affiliated with Canaan Partners[3]	1,733,170	11.7%
Entities affiliated with Frazier Healthcare[4]	1,538,316	10.4%
Entities affiliated with New Leaf Ventures[5]	1,456,303	9.8%
Entities affiliated with Pivotal bioVenture Partners[6]	945,086	6.4%
Entities affiliated with Sofinnova Venture Partners[7]	1,726,514	11.6%
Directors and Named Executive Officers:		
Corey N. Fishman[8]	386,909	2.6%
Michael Dunne, MD[9]	237,732	1.6%
Judith M. Matthews[10]	83,990	*
Brenton K. Ahrens[11]	6,154	*
Mark Chin[2][12]	1,096,057	7.4%
Patrick J. Heron[4][13]	1,544,470	10.4%
Ronald M. Hunt[5][14]	1,467,544	9.9%
David G. Kelly[15]	28,445	*
Shahzad Malik, M.D.[1][16]	879,402	5.9%
All current executive officers and directors as a group (9 persons)[1][2][4][5][17]	5,730,703	37.8%

* less than 1%

(1) Consists of 868,161 shares reported as beneficially owned by Advent Life Sciences LLP, Advent Life Sciences Fund II LP and Shahzad Malik, M.D., of which each such reporting person reports sole voting power with respect to zero of these shares, shared voting power with respect to all 868,161 of these shares, sole dispositive power with respect to zero of these shares and shared dispositive power with respect to all 868,161 of these shares. Advent Life Sciences LLP is the general partner of Advent Life Sciences Fund II LP. Dr. Malik, a member of our board of directors, is a general partner of Advent Life Sciences LLP. The address for each of the reporting persons is 158-160 North Gower Street, London, NW1 2ND, United Kingdom. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13D/A that was filed with the SEC on January 29, 2020.

(2) Consists of 1,089,903 shares beneficially owned by Arix Bioscience Plc, Arix Bioscience Holdings Limited and Mark Chin, of which each such reporting person reports sole voting power with respect to zero of these shares, shared voting power with respect to all 1,089,903 of these shares, sole dispositive power with respect to zero of these shares and shared dispositive power with respect to all 1,089,903 of these shares. The shares are held directly by Arix Bioscience Holdings Limited. Mr. Chin, a member of our board of directors, is an investment director of Arix Bioscience Plc, which is the sole owner and parent of Arix Bioscience Holdings Limited. The address for each of the reporting persons is 20 Berkeley Square, Mayfair, London W1J 6EQ, United Kingdom. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13D/A that was filed with the SEC on January 27, 2020.

(3) Consists of 1,733,170 shares reported as beneficially owned by Canaan X L.P. and Canaan Partners X LLC, of which each such entity reports sole voting power with respect to 1,733,170 shares, shared voting power with respect to zero shares, sole dispositive power with respect to 1,733,170 shares and shared dispositive power with respect to zero shares. The shares are directly held by Canaan X L.P. Canaan Partners X LLC is the general partner of Canaan X L.P. and may be deemed to beneficially own the shares held by Canaan X L.P. Brenton K. Ahrens, Stephen M. Bloch, Daniel T. Ciporin, Wende S. Hutton, Maha S. Ibrahim, Deepak Kamra, Nina Kjellson, Guy M. Russo, Timothy Shannon and Hrach Simonian are the managing members of Canaan Partners X LLC. Investment, voting and dispositive decisions with respect to the shares held by Canaan X L.P. are made by the managers of Canaan Partners X LLC, collectively. Mr. Ahrens, a member of our board of directors, is a managing member of Canaan Partners X LLC. No manager or member of Canaan Partners X LLC has beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act) of any shares held by Canaan X L.P. The address for each of the reporting persons is 285 Riverside Avenue, Suite 250, Westport, Connecticut 06880. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13G that was filed with the SEC on February 6, 2019.

(4) Consists of (a) 1,197,161 shares reported as beneficially owned by Frazier Healthcare VII, L.P., of which such entity reports sole voting power with respect to zero shares, shared voting power with respect to 1,197,161 shares, sole dispositive power with respect to zero shares and shared dispositive power with respect to 1,197,161 shares, and (b) 341,155 shares held directly by Frazier Healthcare VII-A, L.P. of which such entity reports sole voting power with respect to zero shares, shared voting power with respect to 341,155 shares, sole dispositive power with respect to zero shares and shared dispositive power with respect to 341,155 shares. The general partner of Frazier Healthcare VII, L.P. and Frazier Healthcare VII-A, L.P. is FHM VII, L.P., a Delaware limited partnership, and the general partner of FHM VII, L.P. is FHM VII, L.L.C., a Delaware limited liability company, each of which are reported as the beneficial owner of 1,538,316 shares, of which each such entity reports sole voting power with respect to zero shares, shared voting power with respect to 1,538,316 shares, sole dispositive power with respect to zero shares and shared dispositive power with respect to 1,538,316 shares. Mr. Heron, a member of our board of directors, Alan Frazier, Nader Naini, Nathan Every, Brian Morfitt, and James Topper are members of FHM VII, L.L.C. and may be deemed to share voting and investment power with respect to the shares held by FHM VII, L.L.C. The address for each of the reporting persons is c/o Frazier Healthcare Partners, 601 Union Street, Suite 3200, Seattle WA 98101. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13D/A that was filed with the SEC on January 27, 2020.

(5) Consists of (a) 1,071,688 shares reported as beneficially owned by New Leaf Venture III, L.P. (“NLV-III”), New Leaf Venture Associates III, L.P. (“NLVA-III LP”) and New Leaf Venture Management III, L.L.C. (“NLVM-III LLC”), of which each such entity reports sole voting power with respect to 1,071,688 shares, shared voting power with respect to zero shares, sole dispositive power with respect to 1,071,688 shares and shared dispositive power with respect to zero shares, and (b) 384,615 shares held by New Leaf Biopharma Opportunities II, L.P. (“NBPO-II”), New Leaf BPO Associates II, L.P. (“NBPO-IIA”) and New Leaf BPO Management II, L.L.C. (“NBPO-IIM”), of which each such entity reports sole voting power with respect to 384,615 shares, shared voting power with respect to zero shares, sole dispositive power with respect to 384,615 shares and shared dispositive power with respect to zero shares. NLVA-III LP is the general partner of NLV-III and NLVM-III LLC is the general partner of NLVA-III LP. NBPO-IIA is the general partner of NBPO-II and NBPO-IIM is the general partner of NBPO-IIA. Mr. Hunt, a member of our board of directors and Vijay K. Lathi are individual managers of NLVM-III LLC and individual managers of NPBO-IIM , and as a result may be deemed to have shared power to vote and dispose of these shares. The address for each of the reporting persons other

than Vijay K. Lathi is c/o New Leaf Venture Partners, 420 Lexington Avenue, Suite 408, New York, NY 10170. The address for Vijay K. Lathi is c/o New Leaf Venture Partners, 2730 Sand Hill Road, Suite 110, Menlo Park, CA 94025. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13D/A that was filed with the SEC on January 27, 2020.

(6) Consists of 945,086 shares reported as beneficially owned by Pivotal bioVenture Partners Fund I, L.P., Pivotal bioVenture Partners Fund I G.P., L.P. and Pivotal bioVenture Partners Fund I U.G.P., Ltd., of which each such entity reports sole voting power with respect to zero shares, shared voting power with respect to 945,086 shares, sole dispositive power with respect to zero shares and shared dispositive power with respect to 945,086 shares. The shares are held directly by Pivotal bioVenture Partners Fund I, L.P. Pivotal bioVenture Partners Fund I G.P., L.P. is the general partner of Pivotal bioVenture Partners Fund I, L.P. and Pivotal bioVenture Partners Fund I U.G.P., Ltd is the general partner of Pivotal bioVenture Partners Fund I, G.P., L.P. The board of directors of Pivotal bioVenture Partners Fund I U.G.P., Ltd retains ultimate voting and investment control and power over the shares owned by Pivotal bioVenture Partners Fund I, L.P. The address for each of the reporting persons is 1700 Owens Street, Suite 595, San Francisco, CA 94158. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13G that was filed with the SEC on December 24, 2018.

(7) Consists of 1,726,514 shares reported as beneficially owned by Sofinnova Venture Partners IX, L.P. ("SVP IX"), Sofinnova Management IX, L.L.C. ("SM IX"), Dr. Michael F. Powell and Dr. James I. Healy, with respect to which SVP IX and SM IX report sole voting power and sole dispositive power, and Dr. Michael F. Powell and Dr. James I. Healy report shared voting power and shared dispositive power. SM IX is the general partner of SVP IX. Each of Dr. Healy and Michael Powell is a managing member of SM IX. The address for each of the reporting persons is c/o Sofinnova Ventures, 3000 Sand Hill Road, Bldg. 4, Suite 250, Menlo Park, CA 94025. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13D/A that was filed with the SEC on January 24, 2020.

(8) Consists of (a) 239,953 shares held directly by Mr. Fishman, and (b) 146,956 shares issuable to Mr. Fishman pursuant to share options exercisable within 60 days of February 29, 2020.

(9) Consists of (a) 147,958 shares held directly by Dr. Dunne, and (b) 89,774 shares issuable to Dr. Dunne pursuant to share options exercisable within 60 days of February 29, 2020.

(10) Consists of (a) 56,130 shares held directly by Ms. Matthews, and (b) 27,860 shares issuable to Ms. Matthews pursuant to share options exercisable within 60 days of February 29, 2020.

(11) Consists of 6,154 shares beneficially owned by Mr. Ahrens.

(12) Includes 6,154 shares beneficially owned by Mr. Chin.

(13) Includes 6,154 shares held directly by Mr. Heron.

(14) Includes 11,241 shares issuable to Mr. Hunt pursuant to share options exercisable within 60 days of February 29, 2020.

(15) Consists of (a) 25,702 shares beneficially owned by Mr. Kelly and (b) 2,743 shares issuable to Mr. Kelly pursuant to share options exercisable within 60 days of February 29, 2020.

(16) Includes 11,241 shares issuable to Dr. Malik pursuant to share options exercisable within 60 days of February 29, 2020.

(17) I ncludes (a) 488,205 shares held by the current directors and executive officers, (b) 289,815 shares issuable to the current directors and executive officers pursuant to share options exercisable within 60 days of February 29, 2020.

Equity Compensation Plan Information

The following table provides certain aggregage information with respect to all of our equity compensation plans in effect as of December 31, 2019. As of December 31, 2019, we had two equity compensation plans, the 2018 Equity Incentive Plan, or the 2018 Plan, and the 2015 Equity Incentive Plan, or the 2015 Plan, each of which were approved by our shareholders.

Plan category	Number of securities to be issued upon exercise of outstanding options(1)	Weighted average exercise price of outstanding options(2)	Number of securities remaining for future issuance under equity compensation plan (excluding securities reflected in column (a))(3)
Equity compensation plans approved by shareholders	1,231,637	$7.92	537,631
Equity compensation plans not approved by shareholders	—	—	—
Total	1,231,637	$7.92	537,631

(1) This amount includes 31,367 shares subject to outstanding RSUs and 50,000 shares subject to oustanding PSUs, in each case as of December 31, 2019.
(2) The weighted-average exercise price is calculated based solely on the exercise prices of the outstanding options and does not reflect the shares that will be issued upon the vesting of outstanding RSUs and PSUs, which have no exercise price.
(3) The amount disclosed does not reflect an additional 594,758 ordinary shares authorized for issuance under the 2018 Plan as of February 14, 2020, as an annual increase in accordance with the terms of such plan.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The following is a description of transactions since January 1, 2018, to which we have been a party, in which the amount involved exceeds $120,000, and in which any of our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest. We refer to such transactions as "related party transactions" and such persons as "related parties." With the approval of our board of directors, we have engaged in the related party transactions described below. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, from unaffiliated third parties.

Participation in our Initial Public Offering

In May 2018, in our initial public offering, we issued an aggregate of 6,350,000 ordinary shares at a purchase price of $13.00 per share, which included 200,000 ordinary shares issued upon the exercise by the underwriters of their option to purchase additional shares. Certain of our existing shareholders and their affiliated entities, including affiliates of our directors, purchased an aggregate of approximately $42.9 million of our ordinary shares in our initial public offering at the initial public offering price. The table below sets forth the aggregate number of ordinary shares issued to our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, at the time of the transaction:

Name	Shares	Aggregate Purchase Price
Frazier Healthcare VII, L.P.	354,949	$ 4,614,337
Frazier Healthcare VII-A, L.P.	101,150	1,314,950
New Leaf Ventures III, L.P.	278,062	3,614,806
New Leaf Biopharma Opportunities II, L.P.	384,615	4,999,995
Canaan X, L.P.	506,656	6,586,528
Sofinnova Venture Partners IX, L.P.	500,000	6,500,000
Arix Bioscience Holdings Ltd.	337,606	4,388,878
Pivotal bioVenture Partners Fund I, L.P.	313,908	4,080,804
Domain Partners IX, L.P.	153,846	1,999,998
Advent Life Sciences LLP	8,144	105,872
Advent Life Sciences Fund II LP	228,840	2,974,920
Bay City Capital GF Xinde International Life Sciences USD Fund, L.P.	125,563	1,632,319
Corey Fishman	3,000	39,000
Michael Dunne	2,000	26,000
Judith M. Matthews	4,000	52,000
Total	3,302,339	$ 42,930,407

(1) Mr. Heron, a member of our board of directors, is a general partner of Frazier Healthcare Partners
(2) Mr. Hunt, a member of our board of directors, is a managing partner of New Leaf Venture Partners
(3) Mr. Ahrens, a member of our board of directors, is a general partner of Canaan.
(4) Dr. Healy, a former member of our board of directors, is a general partner of Sofinnova Ventures
(5) Mr. Chin, a member of our board of directors, is an investment director of Arix Bioscience
(6) Dr. Hopfner, a former member of our board, is a managing partner of Pivotal bioVenture Partners
(7) Dr. Malik, a member of our board of directors, is a general partner of Advent Life Sciences

Participation in Private Placement

On January 16, 2020, we entered into a Securities Purchase Agreement by and among us, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), Iterum Therapeutics International Limited, Iterum Therapeutics US Limited and Iterum Therapeutics US Holding Limited (collectively, the Guarantors) and a limited number of accredited investors (the Purchasers) pursuant to which Iterum Bermuda sold and issued units consisting of (i) 6.500% Exchangeable Senior Subordinated Notes due 2025 (the Exchangeable Notes), fully and unconditionally guaranteed on an unsecured senior subordinated basis by the Guarantors, and (ii) Limited Recourse Royalty-Linked Subordinated Notes , fully and unconditionally guaranteed on an unsecured senior subordinated basis by the Guarantors (RLNs, and together with the Exchangeable Notes, the Units), to the Purchasers in a private placement (Private Placement). Certain of our existing shareholders and their affiliated entities, including affiliates of our directors, purchased an aggregate of 13,398 Units. The

table below sets forth the aggregate number of Units issued to our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, at the time of the transaction:

Name	Shares	Aggregate Purchase Price
Advent Life Sciences LLP	53	$ 53,000
Advent Life Sciences Fund II LP	1,495	1,495,000
Arix Bioscience Holdings Limited	1,900	1,900,000
Canaan X, L.P.	2,000	2,000,000
Frazier Healthcare VII, L.P.	1,167	1,167,000
Frazier Healthcare VII-A, L.P.	333	333,000
New Leaf Ventures III, L.P.	2,208	2,208,000
New Leaf Biopharma Opportunities II, L.P.	792	792,000
Sofinnova Venture Partners IX, L.P.	1,750	1,750,000
Domain Partners IX, L.P.	1,000	1,000,000
Pivotal bioVenture Partners Fund I, LP	700	700,000
Total	13,398	$ 13,398,000

In connection with the Private Placement, we also entered into an investor rights agreement (the 2020 Investor Rights Agreement) with the Purchasers (including certain of our directors and holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, as listed above) pursuant to which Iterum Bermuda and the Guarantors agreed to file a registration statement covering (a) in the case of a registration statement on Form S-1, the resale of the Exchangeable Notes, the ordinary shares issuable in connection with the exchange of the Exchangeable Notes (the Exchange Shares) and the RLNs or (b) in the case of a registration statement on Form S-3, the Exchange Shares (the securities in (a) and (b) together, the Registrable Securities). Under the 2020 Investor Rights Agreement, we agreed to file an initial registration statement covering the resale by the Purchasers of their Registrable Securities within 10 business days following the later of (x) the earlier of (I) the consummation of an offering of subscription rights to purchase additional Securities that we agreed to undertake in connection with the Private Placement and (II) January 21, 2021and (y) the date on which the number of our unissued ordinary shares available for issuance (less certain reserved shares) is greater than the total number ofordinary shares issuable upon exchange of the then outstanding Exchangeable Notes. If a registration statement has not been filed within the timeframe set forth in the 2020 Investor Rights Agreement or the registration statement covering the Registrable Securities ceases to be effective for resales of Registrable Securities for more than 60 consecutive days or for more than 120 days in any 12-month period, then, subject to the terms of the 2020 Investor Rights Agreement, additional interest will accrue on the Exchangeable Notes and the RLNs.

In addition, pursuant to the terms of the 2020 Investor Rights Agreement, for so long as Sarissa Capital Management LP (Sarissa) and its affiliates own at least 5% or 12.5%, as applicable, of our outstanding ordinary shares on a fully diluted basis, promptly, and in any event no more than 5 business days following written request of Sarissa, we will cause our board of directors to increase to consist of nine or 10 members, as applicable, and we will cause the board of directors to consist of no more than 10 members without the prior written consent of Sarissa. In addition, for so long as Sarissa and its affiliates own at least 12.5% of our outstanding ordinary shares on a fully diluted basis, Sarissa will have the right to designate two directors to our board of directors and, for so long as Sarissa and its affiliates own at least 5% but less than 12.5%, it will have the right to designate one director to our board of directors (Investor Designees). Pursuant to the terms of the 2020 Investor Rights Agreement, such Investor Designees will be appointed to our board of directors and to be members of the class of directors that was subject to reelection at our most recent annual meeting of shareholders. The Investor Designees will be entitled to be a member of any committee of our board of directors subject to the terms of the 2020 Investor Rights Agreement. Pursuant to the terms of the 2020 Investor Rights Agreement, the purchasers party thereto, subject to specified exceptions, have agree with us to vote in favor of the election of the Investor Designees, and we have agreed to cause the Investor Designees to be named in any relevant proxy statement..

Furthermore, pursuant to the terms of the 2020 Investor Rights Agreement, for so long as Sarissa owns 10% of our outstanding ordinary shares on a fully diluted basis, Sarissa will have a right of first offer with respect to future proposed equity financings of ours up to that portion of such new securities which equals Sarissa's percentage ownership of our outstanding ordinary shares on a fully diluted basis, subject to specified exceptions for certain exempt issuances and pursuant to specified procedures. In the event our board of directors determines in good faith that we must conduct an equity financing on an expedited basis without compliance with the right of first offer described above in order to avoid material harm to us or any of our affiliates, we may effect and consummate such equity financing and, as promptly as practicable following the consummation of such equity financing, Sarissa will have the opportunity to participate in such equity financing and be put in the same place (including in respect of the percentage ownership of our equity securities) Sarissa would have been had such equity financing been effected in accordance with the terms of the right of first offer. As set forth in the 2020 Investor Rights Agreement, in any 12 month period, we may conduct an equity financing without compliance with the pre-emptive rights described above (an Excused Issuance); provided that we may not issue new securities (other than specified exempted securities) exceeding (in the aggregate with all other Excused Issuances during such 12 month period) 5% of our issued and outstanding ordinary shares on a fully diluted basis, and we may not issue new securities (other than specified exempted securities) in exchange for consideration (whether in cash or other property) the value of which exceeds (in the aggregate with all other Excused Issuances during such 12 month period) $5.0 million. We may only consummate two Excused Issuances for so long as the 2020 Investor Rights Agreement is in effect.

2017 Investor Rights Agreement

In May 2017, we entered into an amended and restated investor rights agreement with holders of our preferred shares and ordinary shares, including certain holders of more than 5% of our share capital, our executive officers, certain of our directors, and entities affiliated with certain of our directors (the 2017 Investor Rights Agreement). Since the closing of our initial public offering, those holders are entitled to certain registration rights, including the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. The 2017 Investor Rights Agreement also gave the shareholders that are parties thereto the right to participate in new issuances of equity securities by us, subject to certain exceptions. This right to participate in new issuances of equity securities terminated by its terms upon the completion of our initial public offering in May 2018.

Amended Offer Letters

In May 2018 we entered into amended offer letters with certain of our executive officers. For more information regarding these amended offer letters, see *Item 11. Executive Compensation — Employment Agreements with Executive Officers* above.

Equity Grants

We have granted stock option and RSU awards to certain non-employee members of our board of directors. For details and a description of these awards, see *Item 11. Executive Compensation* above.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. In addition, our subsidiary, Iterum Therapeutics US Limited, has entered into an indemnification agreement with each of our directors and executive officers. These agreements, among other things, require us to indemnify an indemnitee to the fullest extent permitted by applicable law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the indemnitee in any action or proceeding, including any action or proceeding by us or in our right, arising out of the person's services as a director or executive officer. We also maintain a directors and officers liability insurance policy which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

Related Party Transaction Policy

We have adopted a formal written policy that our executive officers, directors, key employees, holders of more than 5% of any class of our voting securities, and any member of the immediate family of and any entity affiliated with any of the foregoing persons, are not permitted to enter into a related-party transaction with us without the prior consent of our audit committee, or other independent body of our board of directors in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest. Any request for us to enter into a transaction with an executive officer, director, principal shareholder, or any of their immediate family members or affiliates, in which the amount involved exceeds $120,000, is required to first be presented to our audit committee for review, consideration, and approval. In approving or rejecting any such proposal, our audit committee will consider the relevant facts and circumstances available and deemed relevant to our audit committee, including, but not limited to, whether the transaction will be on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related party's interest in the transaction.

Some of the transactions described in this section were entered into prior to the adoption of this policy. Although we did not have a written policy for the review and approval of transactions with related persons prior to May 2018, our board of directors has historically reviewed and approved any transaction where a director or officer had a financial interest, including the relevant transactions described above. Prior to approving such a transaction, the material facts as to a director's or officer's relationship or interest in the agreement or transaction were disclosed to our board of directors. Our board of directors took this information into account when evaluating the transaction and in determining whether such transaction was fair to us and in the best interest of all our shareholders.

Director independence

Applicable rules of The Nasdaq Stock Market, or Nasdaq, require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq rules require that within one year of the date of the completion of an initial public offering, all the members of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

In order to be considered independent for purposes of Rule 10A-3 under the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

In order to be considered independent for purposes of Rule 10C-1 under the Exchange Act, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including

any consulting, advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In March 2020, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that none of Mr. Ahrens, Mr. Chin, Mr. Heron, Mr. Hunt, Mr. Kelly or Dr. Malik, representing six of our seven current directors, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under Rule 5605(a)(2) of the Nasdaq Marketplace Rules. Mr. Fishman is not an independent director under Rule 5605(a)(2) because he is our President and Chief Executive Officer. Our board of directors has also determined that Messrs. Kelly, Ahrens and Chin, who comprise our audit committee, Messrs. Hunt and Chin and Dr. Malik, who comprise our compensation committee, and Messrs. Heron, Hunt and Kelly and Dr. Malik, who comprise our nominating and corporate governance committee, satisfy the independence standards for such committees established by the SEC and Nasdaq. In making such determination, our board of directors considered the relationships that each such non-employee director has with our Company, including the transactions described in this Item 13, and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our shares by each non-employee director as described above Item 12.

Item 14. Principal Accounting Fees and Services.

The following table presents fees for professional audit services and other services rendered by KPMG to us for the fiscal years ended December 31, 2019 and 2018:

	Year Ended December 31, 2019	Year Ended December 31, 2018
Audit fees (1)	$235,251	$380,070
Audit related fees (2)	—	—
Tax fees (3)	110,758	80,235
All other fees	—	—
	$346,009	$460,305

(1) "Audit Fees" consist of fees billed for professional services performed by KPMG for the audit of our annual financial statements, the review of interim financial statements, and related services that are normally provided in connection with our initial public offering and registration statements on Form S-3 and Form S-8. Included in the 2018 audit fees is $208,427 of fees billed in connection with our initial public offering in May 2018.
(2) "Audit related fees" consist of fees billed by an independent registered public accounting firm for assurance and related services that are reasonably related to the performance of the audit or review of our consolidated financial statements.
(3) "Tax fees" consist of fees for professional services, including tax consulting and compliance performed by an independent registered public accounting firm.

All of these services were pre-approved by the audit committee in accordance with the "*Policy on Audit Committee Pre-Approval of Services*" described below. No work carried out in connection with the audit of our financial statements was performed by persons other than KPMG's full time, permanent employees.

Policy on Audit Committee Pre-Approval of Services

Consistent with SEC policies regarding auditor independence, the audit committee has responsibility for appointing, setting compensation and overseeing the work of our independent registered public accounting firm. In recognition of this responsibility, the audit committee reviews and pre-approves all audit and permissible non-audit services provided by our independent registered public accounting firm; provided, however, that de minimis non-audit services may instead be approved in accordance with applicable SEC rules.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) Consolidated Financial Statements

See Index to Consolidated Financial Statements at Item 8 herein.

(2) Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the consolidated financial statements or notes thereto.

(3) Exhibits

The following is a list of exhibits filed or furnished as part of this Annual Report on Form 10-K;

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
3.1	Constitution of Iterum Therapeutics plc		Form 8-K (Exhibit 3.1)	May 30, 2018	001-38503
4.1	Form of Ordinary Share Certificate of Registrant.		Form S-1 (Exhibit 4.1)	May 1, 2018	333-224582
4.2	Indenture (including form of note), dated January 21, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and U.S. Bank National Association, as trustee.	X			
4.3	Form of 6.500% Exchangeable Senior Subordinated Note due 2025 (included within Exhibit 4.2).	X			
4.4	Indenture (including form of note), dated January 21, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited, Iterum Holders' Representative LLC and Computershare Trust Company, N.A., as trustee.	X			
4.5	Form of Limited Recourse Royalty-Linked Subordinated Note (included within Exhibit 4.4).	X			
4.6	Description of the registrant's registered securities.	X			
10.1†	License Agreement by and among Registrant, Iterum Therapeutics International Limited and Pfizer Inc. dated as of November 18, 2015.		Form S-1 (Exhibit 10.1)	May 1, 2018	333-224582
10.2	Amended and Restated Investor Rights Agreement by and between Registrant and certain of its shareholders dated May 18, 2017.		Form S-1 (Exhibit 10.2)	May 1, 2018	333-224582
10.3+	2015 Equity Incentive Plan.		Form S-1 (Exhibit 10.3)	May 1, 2018	333-224582
10.4+	Forms of U.S. Stock Option Agreement, Stock Option Grant Notice and Notice of Exercise under the 2015 Equity Incentive Plan.		Form S-1 (Exhibit 10.4)	May 1, 2018	333-224582
10.5+	Forms of Irish Stock Option Agreement, Stock Option Grant Notice and Notice of Exercise under the 2015 Equity Incentive Plan.		Form S-1 (Exhibit 10.5)	May 1, 2018	333-224582
10.6+	2018 Equity Incentive Plan.		Form S-1/A (Exhibit 10.6)	May 16, 2018	333-224582
10.7+	Forms of U.S. Stock Option Terms and Conditions and Stock Option Grant Notice under the 2018 Equity Incentive Plan.		Form S-1 (Exhibit 10.7)	May 1, 2018	333-224582
10.8+	Forms of International Stock Option Terms and Conditions and Stock Option Grant Notice under the 2018 Equity Incentive Plan.		Form S-1 (Exhibit 10.8)	May 1, 2018	333-224582
10.9+	Form of Restricted Share Unit Award Agreement under the 2018 Equity Incentive Plan.		Form S-1 (Exhibit 10.9)	May 1, 2018	333-224582
10.10+	Form of 2020 Restricted Share Unit Award Agreement under the 2018 Equity Incentive Plan.	X			
10.12	Form of Indemnity Agreement by and between the Registrant and its directors and officers.		Form S-1 (Exhibit 10.10)	May 1, 2018	333-224582
10.12	Form of Indemnity Agreement by and between Iterum Therapeutics US Limited and its directors and officers.		Form S-1 (Exhibit 10.11)	May 1, 2018	333-224582
10.13+	Employment Terms by and between Iterum Therapeutics US Limited and Corey N. Fishman dated November 18, 2015.		Form S-1 (Exhibit 10.12)	May 1, 2018	333-224582

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
10.14+	Amendment to Employment Agreement by and between Iterum Therapeutics US Limited and Corey N. Fishman dated May 2, 2018.		Form S-1/A (Exhibit 10.13)	May 4, 2018	333-224582
10.15+	Employment Terms by and between Iterum Therapeutics US Limited and Michael W. Dunne dated November 18, 2015.		Form S-1 (Exhibit 10.14)	May 1, 2018	333-224582
10.16+	Employment Terms by and between Iterum Therapeutics US Limited and Judith M. Matthews dated November 18, 2015.		Form S-1 (Exhibit 10.15)	May 1, 2018	333-224582
10.17+	Amendment to Employment Agreement by and between Iterum Therapeutics US Limited and Judith M. Matthews dated May 2, 2018.		Form S-1/A (Exhibit 10.16)	May 4, 2018	333-224582
10.18+	Non-Employee Director Compensation Policy.		Form S-1/A (Exhibit 10.18)	May 16, 2018	333-224582
10.19	Loan and Security Agreement by and among Silicon Valley Bank, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited, and Iterum Therapeutics US Limited, dated April 27, 2018.		Form S-1/A (Exhibit 10.19)	May 4, 2018	333-224582
10.20	Intellectual Property Security Agreement by and among Silicon Valley Bank, the Registrant, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited, and Iterum Therapeutics US Limited, dated April 27, 2018.		Form S-1/A (Exhibit 10.20)	May 4, 2018	333-224582
10.21	Warrant to Subscribe for Shares, issued to Silicon Valley Bank, dated April 27, 2018.		Form S-1/A (Exhibit 10.21)	May 4, 2018	333-224582
10.22	Warrant to Subscribe for Shares, issued to Life Sciences Fund II LLC, dated April 27, 2018.		Form S-1/A (Exhibit 10.22)	May 4, 2018	333-224582
10.23	Additional Form of Warrant to Subscribe for Ordinary Shares as may be issued to Silicon Valley Bank pursuant to the Loan and Security Agreement.		Form S-1/A (Exhibit 10.23)	May 4, 2018	333-224582
10.24	Additional Form of Warrant to Subscribe for Ordinary Shares as may be issued to Life Sciences Fund II LLC pursuant to the Loan and Security Agreement.		Form S-1/A (Exhibit 10.24)	May 4, 2018	333-224582
10.25	Securities Purchase Agreement, dated as of January 16, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and the Investors party thereto.		Form 8-K (Exhibit 10.1)	January 17, 2020	001-38503
10.26	Investor Rights Agreement, dated January 21, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and the Investors party thereto.	X			
10.27	First Amendment to Loan and Security Agreement, dated as of January 16, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and Silicon Valley Bank.		Form 8-K (Exhibit 10.3)	January 17, 2020	001-38503
21.1	Subsidiaries of the Registrant.	X			
23.1	Consent of KPMG, Independent Registered Public Accounting Firm.	X			

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X			
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X			
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X			

_____

+	Indicates management contract or compensatory plan.
†	Confidential treatment has been requested for certain provisions omitted from this Exhibit pursuant to Rule 406 promulgated under the Securities Act. The omitted information has been filed separately with the Securities and Exchange Commission.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

ITERUM THERAPEUTICS PLC

Date: March 12, 2020

By: /s/ Corey N. Fishman
Corey N. Fishman
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ Corey N. Fishman Corey N. Fishman	President and Chief Executive Officer (Principal Executive Officer)	March 12, 2020
/s/ Judith M. Matthews Judith M. Matthews	Chief Financial Officer (Principal Financial and Accounting Officer)	March 12, 2020
/s/ Brenton K. Ahrens Brenton K. Ahrens	Director	March 12, 2020
/s/ Mark Chin Mark Chin	Director	March 12, 2020
/s/ Patrick J. Heron Patrick J. Heron	Director	March 12, 2020
/s/ Ronald M. Hunt Ronald M. Hunt	Director	March 12, 2020
/s/ David G. Kelly David G. Kelly	Director	March 12, 2020
/s/ Shahzad Malik Shahzad Malik, M.D.	Director	March 12, 2020

EXHIBIT 4.2

ITERUM THERAPEUTICS BERMUDA LIMITED,
as Notes Issuer

AND

ITERUM THERAPEUTICS PLC,
ITERUM THERAPEUTICS INTERNATIONAL LIMITED,
ITERUM THERAPEUTICS US LIMITED and
ITERUM THERAPEUTICS US HOLDING LIMITED,

as Guarantors

AND

U.S. BANK NATIONAL ASSOCIATION,

as Trustee

INDENTURE

Dated as of January 21, 2020

6.500% Exchangeable Senior Subordinated Notes due 2025

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EXHIBIT

Exhibit A	Form of Note	A-1

Reconciliation and tie between Trust Indenture Act of 1939 and Indenture, dated as of January 21, 2020.

Trust Indenture Act Section		Agreement Section
Section 310	(a)(1)	7.08
	(a)(2)	7.08
	(a)(3)	Not Applicable
	(a)(4)	Not Applicable
	(a)(5)	7.08
	(b)	7.09, 7.13
	(c)	Not Applicable
Section 311	(a)	7.14
	(b)	7.14
	(c)	Not Applicable
Section 312	(a)	5.01, 5.02(a)
	(b)	5.02(b)
	(c)	5.02(c)
Section 313	(a)	5.03(a)
	(b)	5.03(a)
	(c)	5.03(a), 6.10(b)
	(d)	5.03(b)
Section 314	(a)	4.08, 5.04
	(b)	Not Applicable
	(c)(1)	2.04, 2.05, 2.10, 3.01, 4.04(d), 7.02, 7.07 10.05, 11.03, 14.07(b), 17.05
	(c)(2)	2.10, 3.01, 7.02, 10.05, 11.03, 14.07(b), 17.05
	(c)(3)	Not Applicable
	(d)	Not Applicable
	(e)	17.05
	(f)	Not Applicable
Section 315	(a)	7.01(a), 7.02
	(b)	6.10(b)
	(c)	7.01
	(d)	7.01
	(d)(1)	7.01(a)
	(d)(2)	7.01(b)
	(d)(3)	7.01(c)
	(e)	6.11
Section 316	(a)(last sentence)	8.04

Trust Indenture Act Section		Agreement Section
	(a)(1)(A)	6.09
	(a)(1)(B)	6.09
	(a)(2)	Not Applicable
	(b)	6.06, 6.09
	(c)	8.01
Section 317	(a)(1)	6.04
	(a)(2)	6.04
	(b)	4.04
Section 318	(a)	17.12

Note: This reconciliation and tie shall not, for any purpose, be deemed to be a part of this Indenture.

INDENTURE, dated as of January 21, 2020, among Iterum Therapeutics Bermuda Limited, a company formed under the laws of Bermuda, as Notes Issuer (the "**Company**", as more fully set forth in Section 1.01), Iterum Therapeutics plc, a company formed under the laws of Ireland, as guarantor ("**Iterum**," as more fully set forth in Section 1.01), Iterum Therapeutics International Limited, a company formed under the laws of Ireland, as guarantor (the "**Irish Guarantor**"), Iterum Therapeutics US Limited, a Delaware corporation, as guarantor ("**Iterum U.S. Limited**"), Iterum Therapeutics US Holding Limited, a Delaware corporation, as guarantor ("**Iterum U.S. Holding**" and, together with Iterum, the Irish Guarantor, Iterum U.S. Limited and any guarantor added pursuant to a supplemental indenture in accordance with Section 10.01(c) hereof, the "**Guarantors**") and U.S. BANK NATIONAL ASSOCIATION, a national banking association, as trustee (the "**Trustee**", as more fully set forth in Section 1.01). The Irish Guarantor, Iterum U.S. Limited and Iterum U.S. Holding are referred to herein collectively as the "**Subsidiary Guarantors**".

W I T N E S S E T H:

WHEREAS, for its lawful corporate purposes, the Company has duly authorized the issuance of its 6.500% Exchangeable Senior Subordinated Notes due 2025 (the "**Notes**"), in an aggregate principal amount not to exceed $60,000,000, the Guarantors have duly authorized their issuance of the Guarantee, and in order to provide the terms and conditions upon which the Notes are to be authenticated, issued and delivered, the Company and Iterum have duly authorized the execution and delivery of this Indenture;

WHEREAS, the Form of Note, the certificate of authentication to be borne by each Note, the Form of Notice of Exchange, the Form of Fundamental Change Repurchase Notice and the Form of Assignment and Transfer to be borne by the Notes are to be substantially in the forms hereinafter provided; and

WHEREAS, all acts and things necessary to make the Notes, when executed by the Company and authenticated and delivered by the Trustee or a duly authorized authenticating agent, as provided in this Indenture, the valid, binding and legal obligations of the Company and the Guarantors, and this Indenture a valid agreement according to its terms, have been done and performed, and the execution of this Indenture and the issuance hereunder of the Notes and the Guarantee have in all respects been duly authorized.

NOW, THEREFORE, THIS INDENTURE WITNESSETH:

That in order to declare the terms and conditions upon which the Notes are, and are to be, authenticated, issued and delivered, and in consideration of the premises and of the purchase and acceptance of the Notes by the Holders thereof, each of the Company and the Guarantors covenants and agrees with the Trustee for the equal and proportionate benefit of the respective Holders from time to time of the Notes (except as otherwise provided below), as follows:

ARTICLE 1
Definitions

Section 1.01 *Definitions.* For all purposes of this Indenture, except as expressly provided herein or unless the context otherwise requires:

(a) the terms defined in this Section 1.01 (except as herein otherwise expressly provided or unless the context otherwise requires) for all purposes of this Indenture and of any indenture supplemental hereto shall have the respective meanings specified in this Section 1.01;

(b) all other terms used in this Indenture that are defined in the Trust Indenture Act or the definitions of which in the Securities Act are referred to in the Trust Indenture Act, including terms defined therein by reference to the Securities Act (except as herein otherwise expressly provided or unless the context otherwise clearly requires), shall have the meanings assigned to such terms in the Trust Indenture Act and in the Securities Act as in force at the date of this Indenture;

(c) the words "herein," "hereof," "hereunder," and words of similar import refer to this Indenture as a whole and not to any particular Article, Section or other subdivision;

(d) unless the context otherwise requires, "or" is not inclusive and "including" means "including without limitation"; and

(e) the terms defined in this Article include the plural as well as the singular.

"**Additional Ordinary Shares**" means all Ordinary Shares issued (or, pursuant to Section 14.04(f)(iv), deemed to be issued) by Iterum after the First Issue Date, other than (1) the following Ordinary Shares and (2) Ordinary Shares deemed issued pursuant to the following Options and Convertible Securities (clauses (1) and (2), collectively, "**Exempted Securities**"):

(a) Ordinary Shares, Options or Convertible Securities (including the Notes) issued pursuant to the Rights Offering;

(b) Ordinary Shares, Options or Convertible Securities issued as a dividend or distribution on the Notes;

(c) Ordinary Shares, Options or Convertible Securities issued by reason of a dividend, stock split, split-up, distribution on Ordinary Shares or other transaction;

(d) Ordinary Shares, Options or Convertible Securities issued to employees or directors of, or consultants or advisors to , Iterum or any of its subsidiaries pursuant to a plan, agreement or arrangement approved by the Board of Directors of Iterum or an authorized committee thereof (including, for the avoidance of doubt and without limitation, any Ordinary Shares or Options issued pursuant to Iterum's 2015 Equity

Incentive Plan and 2018 Equity Incentive Plan and any inducement grants made by Iterum pursuant to Nasdaq Listing Rule 5635(c)(4));

(e) Ordinary Shares, Options or Convertible Securities actually issued upon the exercise of Options or Ordinary Shares actually issued upon the conversion or exchange of Convertible Securities (including the Notes) , in each case provided such issuance is pursuant to the terms of such Option or Convertible Security;

(f) Ordinary Shares, Options or Convertible Securities issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction;

(g) Ordinary Shares, Options or Convertible Securities issued to suppliers or third- party service providers in connection with the provision of goods or services pursuant to transactions with such third-parties or their Affiliates;

(h) Ordinary Shares, Options or Convertible Securities issued as acquisition consideration pursuant to the acquisition of another entity by Iterum, the Company or any Guarantor by merger, purchase of substantially all of the assets, the acquisition of assets of another entity by Iterum, the Company or any Guarantor, other reorganization or to a joint venture agreement; or

(i) Ordinary Shares, Options or Convertible Securities issued in connection with sponsored research, collaboration, technology license, development, manufacturing, supply, distribution, marketing or other similar commercial agreements or strategic partnerships.

"**Affiliate**" of any specified Person means any other Person directly or indirectly controlling or controlled by or under direct or indirect common control with such specified Person. For the purposes of this definition, "control," when used with respect to any specified Person means the power to direct or cause the direction of the management and policies of such Person, directly or indirectly, whether through the ownership of voting securities, by contract or otherwise; and the terms "controlling" and "controlled" have meanings correlative to the foregoing.

"**Aggregate Ownership Cap**" has the meaning set forth in Section 14.01(c)(ii).

"**Applicable Tax Law**" shall have the meaning specified in Section 4.10.

"**Authorized Shares Approval**" means such approvals as may be required from Iterum's shareholders (i) to increase the authorized number of Ordinary Shares under Iterum's Constitution such that the number of unissued Ordinary Shares that are available for issuance by Iterum (excluding any shares that are issuable upon exercise, conversion or exchange of outstanding options, warrants or other securities or are reserved under any equity incentive plan maintained by Iterum) is greater than the total number of Ordinary Shares that are issuable upon exchange of the then-outstanding Notes (disregarding any limitations on exchange in Section

14.01(c)) and (ii) to amend Article 7 of Iterum's Articles of Association to authorize Iterum's Board of Directors to allot and issue such newly created Ordinary Shares generally and to do so on a non pre-emptive basis as if Section 1022 of the Irish Companies Act 2014 did not apply.

"**Available Shares**" means a number of Ordinary Shares equal to the number of authorized but unissued Ordinary Shares that are available for issuance by Iterum (excluding any shares that are issuable upon exercise, conversion or exchange of outstanding options, warrants or other securities or are reserved under any equity plan maintained by Iterum or reserved for exchange of any Notes issued pursuant to the Rights Offering).

"**Available Shares Ownership Cap**" has the meaning set forth in Section 14.01(c)(iii).

"**Bankruptcy Code**" means Title 11 of the United States Code.

"**Bankruptcy Law**" means the Bankruptcy Code (or any successor thereto) or any similar bankruptcy, insolvency or other U.S. federal or state law, or similar foreign law (including under Bermudan or Irish law), for the relief of debtors, whether now or hereafter in effect.

"**Beneficial Holder**" has the meaning set forth in Section 2.05(c).

"**Benefited Party**" shall have the meaning specified in Section 13.01(b).

"**Board of Directors**" means, with respect to the Company or any Guarantor, the board of directors (or equivalent governing body) of the Company or such Guarantor, as the case may be, or a committee of such board duly authorized to act for it hereunder.

"**Board Resolution**" means a copy of a resolution certified by the Secretary or an Assistant Secretary of the Company or any Guarantor, as the case may be, to have been duly adopted by the applicable Board of Directors, and to be in full force and effect on the date of such certification, and delivered to the Trustee.

"**Business Day**" means, with respect to any Note, any day other than (a) a Saturday, (b) a Sunday, (c) a day on which the Federal Reserve Bank of New York or banking institutions in London or Bermuda are authorized or required by law or executive order to close or be closed or (d) solely for purposes of Section 17.06, a day on which banking institutions in the location of the Trustee or Paying Agent, as the case may be, are authorized or required by law to close.

"**Cap**" shall have the meaning specified in Section 2.01.

"**Capital Stock**" means, for any Person, any and all shares, interests, rights to purchase, warrants, options, participations or other equivalents of or interests in (however designated)

stock or shares issued by that Person, but excluding any debt securities convertible or exchangeable into such stock or shares.

"**Cash Equivalents**" means (a) marketable direct obligations issued or unconditionally guaranteed by the United States or any agency or any State thereof having maturities of not more than one (1) year from the date of acquisition; (b) commercial paper maturing no more than one (1) year after its creation and having the highest rating from either Standard & Poor's Ratings Group or Moody's Investors Service, Inc., with an aggregate market value not in excess of $18,750,000, provided that there are no legal or market impediments to the immediate sale of such commercial paper; (c) certificates of deposit maturing no more than one (1) year after issue; and (d) money market funds at least ninety-five percent (95%) of the assets of which constitute Cash Equivalents of the kinds described in clauses (a) through (c) of this definition. Notwithstanding the foregoing, Cash Equivalents does not include purchasing participations in, entering into any type of swap or other equivalent derivative transaction, or otherwise holding or engaging in any ownership interest in any type of debt instrument, including, without limitation, any corporate or municipal bonds with a long-term nominal maturity for which the interest rate is reset through a dutch auction and more commonly referred to as an auction rate security.

"**Cash Settlement**" shall have the meaning specified in Section 14.02(a).

"**Change of Control Price**" means, with respect to a Note, the greater of (i) 300% of the principal amount thereof, and (ii) the consideration that would be received by the Holder of such Note in connection with a Change of Control Transaction if the Holder had exchanged the Note for Ordinary Shares immediately prior to the consummation of such Change of Control Transaction.

For the purpose of determining the value of non-cash consideration received in such a Change of Control Transaction, the value of such consideration shall be deemed to be the fair market value of such consideration. The determination of fair market value of such property shall be made in good faith by the Board of Directors of Iterum, provided that to the extent such property consists of securities, the fair market value of such securities shall be determined as follows:

a) if traded on a national securities exchange or the Nasdaq Stock Market (or a similar national quotation system), the value shall be deemed to be the average closing prices of the securities on such exchange or system for the 30 trading days immediately prior to the closing of such Change of Control Transaction;

b) if actively traded over-the-counter, the value shall be deemed to be the average of the closing bid or sale prices (whichever is applicable) for the 30 trading days immediately prior to the closing of such Change of Control Transaction; or

c) if there is no active public market, the value shall be the fair market value thereof, as determined in good faith by the Board of Directors of Iterum.

For the purposes of this definition only, "**trading day**" means any day which the exchange or system on which the securities to be distributed are traded is open and "**closing prices**" or "**closing bid or sales prices**" shall be deemed to be: (A) for securities traded primarily on the New York Stock Exchange or Nasdaq Stock Market, the last reported trade price or sale price, as the case may be, at 4:00 p.m., New York time, on that day and (B) for securities listed or traded on other exchanges, markets and systems, the market price as of the end of the regular hours trading period that is generally accepted as such for such exchange, market or system.

"**Change of Control Transaction**" means any transaction that constitutes a Fundamental Change pursuant to clause (a) or clause (b) of the definition thereof.

"**Clause A Distribution**" shall have the meaning specified in Section 14.04(c).

"**Clause B Distribution**" shall have the meaning specified in Section 14.04(c).

"**Clause C Distribution**" shall have the meaning specified in Section 14.04(c).

"**close of business**" means 5:00 p.m. (New York City time).

"**Code**" means the U.S. Internal Revenue Code of 1986, as amended.

"**Combination Settlement**" shall have the meaning specified in Section 14.02(a).

"**Commission**" means the U.S. Securities and Exchange Commission, as from time to time constituted, created under the Exchange Act, or if at any time after the execution and delivery of this Indenture such Commission is not existing and performing the duties now assigned to it under the Trust Indenture Act, then the body performing such duties on such date.

"**Common Equity**" of any Person means Capital Stock of such Person that is generally entitled (a) to vote in the election of directors of such Person or (b) if such Person is not a corporation, to vote or otherwise participate in the selection of the governing body, partners, managers or others that will control the management or policies of such Person.

"**Company**" shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns. To the extent necessary to comply with the requirements of the provisions of Trust Indenture Act Sections 310 through 317, inclusive, to the extent that they are applicable to the Company, the term "Company" shall include any other obligor with respect to the Notes for the purposes of complying with such provisions.

"**Company Order**" means a written order of the Company, signed by (a) the Company's Chief Executive Officer, Chief Financial Officer or President or any director of the Company,

and (b) any such other Officer designated in clause (a) of this definition or the Company's Secretary or any Assistant Secretary, and delivered to the Trustee.

"**Convertible/Redeemable Securities**" shall have the meaning specified in Section 4.11(b).

"**Convertible Securities**" means any evidences of indebtedness, shares or other securities that by their terms are directly or indirectly convertible into or exchangeable for Ordinary Shares, but excluding Options and the Notes.

"**Corporate Trust Office**" means the designated office of the Trustee at which at any time its corporate trust business shall be administered, which office at the date hereof is located (i) solely for purposes of surrender for registration, transfer, exchange, presentation for payment or repurchase, or conversion, at U.S. Bank National Association, 111 Fillmore Avenue, St. Paul, MN 55107, Attention: Global Corporate Trust Services – Iterum Therapeutics, PLC, and (ii) for all other purposes, at U.S. Bank National Association, 225 Asylum Street, 23rd Floor, Hartford, CT 06103, Attention: Global Corporate Trust Services – Iterum Therapeutics, PLC, or such other address as the Trustee may designate from time to time by notice to the Holders and the Company, or the designated corporate trust office of any successor trustee (or such other address as such successor trustee may designate from time to time by notice to the Holders and the Company).

"**Custodian**" means the Trustee, as custodian for The Depository Trust Company, with respect to the Global Notes, or any successor entity thereto.

"**Daily Exchange Value**" means, for each of the 30 consecutive Trading Days during the Observation Period, one-thirtieth of the product of (a) the Exchange Rate on such Trading Day and (b) the Daily VWAP on such Trading Day.

"**Daily Measurement Value**" means the Specified Dollar Amount (if any), *divided by* 30.

"**Daily Settlement Amount**," for each of the 30 consecutive Trading Days during the Observation Period, shall consist of:

(a) cash in an amount equal to the lesser of (i) the Daily Measurement Value and (ii) the Daily Exchange Value on such Trading Day; and

(b) if the Daily Exchange Value on such Trading Day exceeds the Daily Measurement Value, a number of Ordinary Shares equal to (i) the difference between the Daily Exchange Value and the Daily Measurement Value, *divided by* (ii) the Daily VWAP for such Trading Day.

"**Daily VWAP**" means, for any Trading Day, the per share volume-weighted average price of the Ordinary Shares as displayed under the heading "Bloomberg VWAP" on Bloomberg page "ITRM <equity> AQR" (or its equivalent successor if such page is not available) in respect of the period from the scheduled open of trading until the scheduled close of trading of the primary trading session on such Trading Day (or if such volume-weighted average price is unavailable, the market value of one Ordinary Share on such Trading Day determined, using a volume-weighted average method, by a nationally recognized independent investment banking firm retained for this purpose by the Company). The "**Daily VWAP**" shall be determined without regard to after-hours trading or any other trading outside of the regular trading session trading hours.

"**Default**" means any event that is, or after notice or passage of time, or both, would be, an Event of Default.

"**Defaulted Amounts**" means any amounts on any Note (including the Redemption Price, the Fundamental Change Repurchase Price, principal and interest) that are payable but have not been paid or duly provided for.

"**Depositary**" means, with respect to each Global Note, the Person specified in Section 2.05(c) as the Depositary with respect to such Notes, until a successor shall have been appointed and become such pursuant to the applicable provisions of this Indenture, and thereafter, "**Depositary**" shall mean or include such successor.

"**Distributed Property**" shall have the meaning specified in Section 14.04(c).

"**Effective Date**", as used in Section 14.04, means the first date on which Ordinary Shares trade on the applicable exchange or in the applicable market, regular way, reflecting the relevant share split or share combination, as applicable.

"**Event of Default**" shall have the meaning specified in Section 6.01.

"**Ex-Dividend Date**" means the first date on which Ordinary Shares trade on the applicable exchange or in the applicable market, regular way, without the right to receive the issuance, dividend or distribution in question, from Iterum or, if applicable, from the seller of Ordinary Shares on such exchange or market (in the form of due bills or otherwise) as determined by such exchange or market. For the avoidance of doubt, any alternative trading convention on the applicable exchange or market in respect of the Ordinary Shares under a separate ticker symbol or CUSIP will not be considered "regular way" for this purpose.

"**Exchange Act**" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

"**Exchange Agent**" shall have the meaning specified in Section 4.02.

"**Exchange Date**" shall have the meaning specified in Section 14.02(c).

"**Exchange Obligation**" means the Company's obligation to deliver the consideration payable upon an exchange pursuant to Section 14.01(a) or Section 14.01(b), subject to, and in accordance with, the settlement provisions of Section 14.02.

"**Exchange Price**" means as of any date, $1,000, divided by the Exchange Rate as of such date.

"**Exchange Rate**" shall have the meaning specified in Section 14.01(a).

"**Exchange Settlement Date**" shall have the meaning specified in Section 14.02(c).

"**Exempted Securities**" shall have the meaning specified in the definition of Additional Ordinary Shares.

"**First Issue Date**" means the original issuance date of the first Notes issued pursuant to this Indenture.

"**Form of Assignment and Transfer**" means the "Form of Assignment and Transfer" attached as Attachment 3 to the Form of Note attached hereto as Exhibit A.

"**Form of Fundamental Change Repurchase Notice**" means the "Form of Fundamental Change Repurchase Notice" attached as Attachment 2 to the Form of Note attached hereto as Exhibit A.

"**Form of Note**" means the "Form of Note" attached hereto as Exhibit A.

"**Form of Notice of Exchange**" means the "Form of Notice of Exchange" attached as Attachment 1 to the Form of Note attached hereto as Exhibit A.

"**Fundamental Change**" shall be deemed to have occurred at the time after the Notes are originally issued if any of the following occurs:

(a) a "person" or "group" within the meaning of Section 13(d) of the Exchange Act, other than any of (w) the Company, (x) Iterum, (y) the Subsidiary Guarantors and their wholly owned Subsidiaries and (z) the employee benefit plans of Iterum and its wholly owned Subsidiaries, files a Schedule TO or any schedule, form or report under the Exchange Act disclosing that such person or group has become the direct or indirect "beneficial owner," as defined in Rule 13d-3 under the Exchange Act, of Iterum's Common Equity representing more than 50% of the aggregate voting power of Iterum's Common Equity; provided that the Holders of Specified Notes shall not be

considered a "person" or "group" within the meaning of Section 13(d) of the Exchange Act by virtue of the rights and obligations set forth in the Investor Rights Agreement.

(b) the consummation of (i) any recapitalization, reclassification or change of the Ordinary Shares (other than changes resulting from a subdivision or combination) as a result of which the Ordinary Shares would be converted into, or exchanged for, capital stock, other securities, other property or assets; (ii) any share purchase, share exchange, consolidation or merger or other similar transaction involving Iterum pursuant to which the Ordinary Shares will be converted into cash, securities or other property or assets; or (iii) any sale, lease or other transfer in one transaction or a series of related transactions of all or substantially all of the consolidated assets (including intellectual property) of Iterum and its Subsidiaries, taken as a whole, to any Person other than one of Iterum's wholly owned Subsidiaries; *provided*, *however*, that neither (A) a transaction described in clause (ii) in which the holders of all classes of Iterum's Common Equity immediately prior to such transaction own, directly or indirectly, more than 50% of all classes of Common Equity of the continuing or surviving Person or transferee or the parent thereof immediately after such transaction in substantially the same proportions as such ownership immediately prior to such transaction nor (B) any merger or consolidation of Iterum solely for the purpose of changing Iterum's jurisdiction of incorporation that results in a reclassification, conversion or exchange of issued Ordinary Shares solely into shares of common stock of the surviving Person, shall be a Fundamental Change pursuant to this clause (b);

(c) the stockholders of the Company, Iterum or the Irish Guarantor approve any plan or proposal for the liquidation or dissolution of the Company, Iterum or the Irish Guarantor; or

(d) the Ordinary Shares cease to be listed on any Permitted Exchange.

provided, *however*, that any transaction that constitutes a Fundamental Change pursuant to both clause (a) and clause (b) above shall be deemed a Fundamental Change solely under clause (b) above; and *provided*, *further*, that a transaction or transactions described in clause (a) or clause (b) above shall not constitute a Fundamental Change pursuant to clause (a) or (b) above if at least 90% of the consideration received or to be received by the common stockholders of Iterum, excluding cash payments for fractional shares or pursuant to dissenters' rights, in connection with such transaction or transactions consists of shares of common stock that are listed or quoted on any Permitted Exchange or will be so listed or quoted when issued or exchanged in connection with such transaction or transactions and as a result of such transaction or transactions the Notes become convertible or exchangeable into such consideration, excluding cash payments for fractional shares (subject to the provisions of Section 14.02). If any transaction in which the Ordinary Shares are replaced by the securities of another entity occurs,

following the effective date of such transaction, references to Iterum in this definition shall instead be references to such other entity.

"**Fundamental Change Company Notice**" shall have the meaning specified in Section 15.02(c).

"**Fundamental Change Repurchase Date**" shall have the meaning specified in Section 15.02(a).

"**Fundamental Change Repurchase Notice**" shall have the meaning specified in Section 15.02(b)(i).

"**Fundamental Change Repurchase Price**" shall have the meaning specified in Section 15.02(a).

"**GAAP**" means U.S. generally accepted accounting principles as in effect from time to time.

"**Global Note**" shall have the meaning specified in Section 2.05(b).

"**Guarantee**" means the guarantee of the Company's obligations under this Indenture and the Notes, issued by the Guarantors pursuant to Article 13 of this Indenture.

"**Guarantee Obligations**" shall have the meaning specified in Section 13.01(a).

"**Guarantors**" shall have the meaning specified in the first paragraph of this Indenture.

"**Guarantor Senior Debt**" means all obligations of any Guarantor to Silicon Valley Bank now existing or hereafter arising, including, without limitation, (i) the Obligations (as defined in the SVB Facility), together with all costs of collecting such obligations (including attorneys' fees), (ii) all obligations now existing or hereafter arising under any agreement in connection with the provision by Silicon Valley Bank to any Guarantor of products and/or credit services facilities, including, without limitation, any letters of credit, cash management services (including, without limitation, merchant services, direct deposit of payroll, business credit cards, and check cashing services), interest rate swap arrangements, and foreign exchange services, (iii) all interest accruing after the commencement by or against any Guarantor of any bankruptcy, reorganization or similar proceeding, whether or not a claim for post-petition interest is allowed as a claim in the proceeding and (iv) any obligations of the Guarantors hereafter arising that the applicable Guarantor(s) designate as "Guarantor Senior Debt"; provided, however, that the aggregate principal amount of any such indebtedness constituting Guarantor Senior Debt shall not exceed $50,000,000 outstanding at any time (it being understood that the maximum amount of Guarantor Senior Debt is not additive to the maximum amount of Senior Debt but instead

refers to the same maximum amount as applied to each Guarantor with respect to Guarantor Senior Debt and to the Company with respect to Senior Debt).

"**Holder**," as applied to any Note, or other similar terms (but excluding the term "beneficial holder"), means any Person in whose name at the time a particular Note is registered on the Note Register.

"**Indenture**" means this instrument as originally executed or, if amended or supplemented as herein provided, as so amended or supplemented.

"**Indebtedness**" means (a) indebtedness for borrowed money or the deferred price of property or services, such as reimbursement and other obligations for surety bonds and letters of credit, (b) obligations evidenced by notes, bonds, debentures or similar instruments, and (c) any lease obligation that is required to be accounted for as a finance lease in accordance with GAAP.

"**Individual Ownership Cap**" has the meaning set forth in Section 14.01(c)(i).

"**Initial Purchasers**" means Advent Life Sciences LLP, Advent Life Sciences Fund II LP, Arix Bioscience Holdings Limited, Canaan X L.P., Frazier Healthcare VII, L.P., Frazier Healthcare VII-A, L.P., New Leaf Ventures III, L.P., New Leaf Biopharma Opportunities II, L.P., Sofinnova Venture Partners IX, L.P., Domain Partners IX, L.P., Pivotal bioVenture Partners Fund I, LP, Sarissa Capital Offshore Master Fund LP, Sarissa Capital Catapult Fund LLC, Sarissa Capital Hawkeye Fund LP, RA Capital Healthcare Fund, L.P., Blackwell Partners LLC – Series A, Empery Master Onshore, LLC, Empery Tax Efficient, LP, Empery Tax Efficient II, LP, Lincoln Park Capital Fund, LLC, 683 Capital Partners, LP, SilverArc Capital Alpha Fund I, L.P., SilverArc Capital Alpha Fund II, L.P., 2b LLC, Sabby Volatility Warrant Master Fund, Ltd., S.H.N Financial investments ltd, North Sound Trading, LP, CVI Investments, Inc., Salthill Investors (Bermuda) L.P., Salthill Partners, L.P. and Gary D. Cohn.

"**Interest Payment Date**" means the Maturity Date.

"**Interest Record Date**" means January 15, 2025 (whether or not such day is a Business Day).

"**Investor Rights Agreement**" means the Investor Rights Agreement, dated as of January 21, 2020, among the Company and the Initial Purchasers.

"**Irish Guarantor**" shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns.

"**Irish Takeover Rules**" means The Irish Takeover Panel Act 1997, Takeover Rules 2013.

"**Iterum**" shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns.

"**Iterum U.S. Holding**" shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns.

"**Iterum U.S. Limited**" shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns.

"**IV Product**" means the sulopenem antibiotic being developed by Iterum for intravenous delivery.

"**Last Reported Sale Price**" of the Ordinary Shares on any Trading Day means the closing sale price per share (or if no closing sale price is reported, the average of the bid and ask prices or, if more than one in either case, the average of the average bid and the average ask prices) on that Trading Day as reported in composite transactions for the principal U.S. national or regional securities exchange on which the Ordinary Shares are traded. If the Ordinary Shares are not listed for trading on a U.S. national or regional securities exchange on the relevant date, the "**Last Reported Sale Price**" shall be the last quoted bid price for the Ordinary Shares in the over-the-counter market on the relevant date as reported by OTC Markets Group Inc. or a similar organization. If the Ordinary Shares are not so quoted, the "**Last Reported Sale Price**" shall be the average of the mid-point of the last bid and ask prices for the Ordinary Shares on the relevant date from each of at least three nationally recognized independent investment banking firms selected by the Company for this purpose.

"**Liquidation Event**" means an event described in clause (c) of the definition of Fundamental Change.

"**Major Investors**" means Sarissa Capital Offshore Master Fund LP, Sarissa Capital Catapult Fund LLC and Sarissa Capital Hawkeye Fund LP and their respective successors.

"**Mandatory Exchange**" shall have the meaning specified in Section 14.01(b).

"**Mandatory Exchange Notice**" shall have the meaning specified in Section 14.01(b).

"**Mandatory Exchange Trigger Event**" means the first date, following January 21, 2021 and on or prior to January 1, 2025, on which (A) the U.S. Food and Drug Administration has accepted for filing a new drug application and, if applicable, a supplemental new drug application (or, in each case, any successor form or application having substantially the same effect with respect to the approval of a drug for marketing and sale) by Iterum or any of its Affiliates for the Products in respect of each of the following indications: uncomplicated urinary tract infection and complicated urinary tract infection; (B) Iterum has at least $75 million of Unrestricted Cash, on a consolidated basis, without including any net proceeds from sales of the

Notes and the RLNs to the Initial Purchasers and any other financing provided by the Initial Purchasers to Iterum or any of its Subsidiaries after the date of this Indenture; and (C) the Daily VWAP of the Ordinary Shares shall have been at least $8.00 (subject to adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization) on each Trading Day during the 60 consecutive Trading Days immediately preceding the date of determination.

"**Market Disruption Event**" means, for the purposes of determining amounts due upon exchange (i) a failure by the primary U.S. national or regional securities exchange or market on which the Ordinary Shares are listed or admitted for trading to open for trading during its regular trading session; or (ii) the occurrence or existence prior to 1:00 p.m., New York City time, on any Scheduled Trading Day for the Ordinary Shares for more than one half-hour period in the aggregate during regular trading hours of any suspension or limitation imposed on trading (by reason of movements in price exceeding limits permitted by the relevant stock exchange or otherwise) in the Ordinary Shares or in any options contracts or futures contracts relating to the Ordinary Shares.

"**Maturity Date**" means January 31, 2025.

"**Note**" or "**Notes**" shall have the meaning specified in the first paragraph of the recitals of this Indenture.

"**Note Register**" shall have the meaning specified in Section 2.05(a).

"**Note Registrar**" shall have the meaning specified in Section 2.05(a).

"**Notice of Exchange**" shall have the meaning specified in Section 14.02(b).

"**Observation Period**" with respect to any Note surrendered for exchange means: (i) subject to clause (ii), if the relevant Exchange Date occurs prior to October 31, 2024, the 30 consecutive Trading Day period beginning on, and including, the second Trading Day immediately succeeding such Exchange Date; (ii) if the relevant Exchange Date occurs on or after the date of the Company's issuance of a Redemption Notice with respect to the Notes pursuant to Section 16.02 and prior to the close of business on the second Scheduled Trading Day immediately preceding the relevant Redemption Date, the 30 consecutive Trading Days beginning on, and including, the 31st Scheduled Trading Day immediately preceding such Redemption Date; and (iii) subject to clause (ii), if the relevant Exchange Date occurs on or after October 31, 2024, the 30 consecutive Trading Days beginning on, and including, the 31st Scheduled Trading Day immediately preceding the Interest Record Date.

"**Officer**" means, (i) with respect to the Company, the Company's President, Chief Executive Officer, Chief Financial Officer or Secretary or any director of the Company, (ii) with respect to Iterum, Iterum's President, Chief Executive Officer, Chief Financial Officer, Secretary, Treasurer or any director of Iterum and (iii) with respect to any Subsidiary Guarantor,

such Subsidiary Guarantor's President, Chief Executive Officer, Chief Financial Officer, Secretary or Treasurer, any director of such Subsidiary Guarantor, or any attorney appointed by such entity.

"**Officer's Certificate**," when used with respect to the Company or any Guarantor, means a certificate that is delivered to the Trustee and that is signed by an Officer of the Company or such Guarantor, as applicable. Each such certificate shall comply with Section 314 of the Trust Indenture Act and, except to the extent provided herein, shall include the statements provided for in Section 17.05 if and to the extent required by the provisions of such Section. The Officer giving an Officer's Certificate pursuant to Section 4.08 shall be the principal executive, financial or accounting officer of the Company.

"**open of business**" means 9:00 a.m. (New York City time).

"**Opinion of Counsel**" means an opinion in writing signed by legal counsel, who may be an employee of or counsel to the Company, Iterum or any of the Subsidiary Guarantors, as applicable, or other counsel that is acceptable to the Trustee, that is delivered to the Trustee, which opinion may contain customary exceptions and qualifications as to the matters set forth therein and which legal counsel may, in providing such opinion, rely upon certifications or other representations as to matters of fact. Each such opinion shall comply with Section 314 of the Trust Indenture Act and include the statements provided for in Section 17.05 if and to the extent required by the provisions of such Section 17.05.

"**Optional Redemption**" shall have the meaning specified in Section 16.01.

"**Option**" means rights, options or warrants to purchase or otherwise acquire Ordinary Shares or Convertible Securities.

"**Oral Product**" means sulopenem etzadroxil and probenecid combined in a single bilayer tablet being developed by Iterum for oral administration.

"**Ordinary Shares**" means the ordinary shares of Iterum, nominal value $0.01 per share, at the date of this Indenture, subject to adjustment after the date of this Indenture pursuant to Section 14.07.

"**outstanding**," when used with reference to the Notes, shall, subject to the provisions of Section 8.04, mean, as of any particular time, all Notes authenticated and delivered by the Trustee under this Indenture, except:

(a) Notes theretofore canceled by the Trustee or accepted by the Trustee for cancellation;

(b) Notes, or portions thereof, that have become due and payable and in respect of which monies in the necessary amount shall have been deposited in trust with the Trustee or with any Paying Agent (other than the Company) or shall have been set aside and segregated in trust by the Company (if the Company shall act as its own Paying Agent);

(c) Notes that have been paid pursuant to Section 2.06 or Notes in lieu of which, or in substitution for which, other Notes shall have been authenticated and delivered pursuant to the terms of Section 2.06 unless proof satisfactory to the Trustee is presented that any such Notes are held by protected purchasers in due course;

(d) Notes exchanged pursuant to Article 14 and required to be cancelled pursuant to Section 2.08; and

(e) Notes repurchased by the Company or the Guarantors pursuant to the penultimate sentence of Section 2.10.

"**Paying Agent**" shall have the meaning specified in Section 4.02.

"**Permitted Exchange**" means The New York Stock Exchange, The NYSE American, The Nasdaq Global Select Market, The Nasdaq Global Market, the Nasdaq Capital Market (or any of their respective successors) or any Designated Offshore Securities Market (as defined in Rule 902 under the Securities Act).

"**Permitted Indebtedness**" means:

(a) the Guarantors' and the Company's Indebtedness to the Holders pursuant to this Indenture (subject in all cases to the Cap) and the Notes and any Indebtedness in respect of the RLNs;

(b) the Guarantors' and any of their Subsidiaries' debt or credit facilities, including (i) the SVB Facility, and any replacement, restatement, refunding, refinancing, amendment, supplement, modification, extension or renewal thereof whether by the same or any other agent, lender or group of lenders, (ii) additional Indebtedness incurred under the SVB Facility or any replacement, restatement, refunding, refinancing, amendment, supplement, modification, extension or renewal thereof whether by the same or any other agent, lender or group of lenders, and (iii) any other Indebtedness for borrowed money, including any financing arrangements (including commercial paper facilities or indentures) providing for revolving credit loans, term loans, letters of credit or other long-term indebtedness, including any notes, mortgages, guarantees, collateral documents, instruments and agreements executed in connection therewith, and any replacement, restatement, refunding, refinancing, amendment, supplement, modification, extension or renewal thereof whether by the same or any other agent, lender or group of

lenders; provided that the aggregate principal amount of Indebtedness permitted to be outstanding under this clause (b) shall not exceed Fifty Million Dollars ($50,000,000);

(c) Subordinated Indebtedness incurred by the Guarantors or any of their Subsidiaries; provided that the aggregate principal amount of Indebtedness permitted to be outstanding under this clause (c) shall not exceed $15,000,000;

(d) unsecured Indebtedness owed to trade creditors incurred by the Guarantors or any of their Subsidiaries in the ordinary course of business;

(e) Indebtedness consisting of finance lease obligations (in accordance with GAAP), equipment financing and purchase money Indebtedness, in each case incurred by the Guarantors or one of their Subsidiaries to finance the acquisition, repair, improvement or construction of fixed or capital assets of such person; provided that the aggregate principal amount of Indebtedness permitted to be outstanding under this clause (e) shall not exceed $15,000,000;

(f) any obligations with respect to (i) corporate credit cards issued for the account of the Guarantors or any of their Subsidiaries in the ordinary course of business, (ii) any interest rate, currency or commodity swap agreement, interest rate cap agreement, interest rate collar agreement, or other agreement or arrangement designated to protect the Guarantors or any of their Subsidiaries against fluctuation in interest rates, currency exchange rates or commodity prices and not used for speculative purposes, or (iii) letters of credit, bank guarantees, bankers' acceptances, warehouse receipts and similar instruments issued for the account of the Guarantors or any of their Subsidiaries in the ordinary course of business for the purposes of (A) workers' compensation claims, health, disability and other employee benefits, property, casualty and liability insurance and self-insurance, unemployment insurance, and other social security laws, and (B) bids, trade contracts, leases, statutory obligations, surety and appeal bonds, performance bonds, completion guarantees and obligations of a like nature;

(g) deposits held in escrow accounts or held by landlords, for real estate leases issued for the account of the Guarantors or any of their Subsidiaries in the ordinary course of business;

(h) (i) Indebtedness owed by the Company or the Guarantors to one of their wholly-owned Subsidiaries, (ii) Indebtedness owed to the Company or the Guarantors by one of their wholly-owned Subsidiaries and (iii) Indebtedness owed by a Guarantor to another Guarantor or the Company;

(i) Indebtedness of the Guarantors or one of their Subsidiaries consisting of the financing of insurance premiums in the ordinary course of business;

(j) unsecured Indebtedness in the form of "Regulatory Approval Milestone Payments" owing to Pfizer Inc. arising out of, related to or in any way in connection with the Pfizer License, or otherwise (including but not limited to any unsecured promissory notes issued to Pfizer Inc. in accordance with Section 5.4 of the Pfizer License), plus accrued or capitalized interest thereon;

(k) [reserved];

(l) Indebtedness arising from agreements of the Guarantors or one of their Subsidiaries entered into in accordance with the terms of this Indenture, providing for indemnification, adjustment of purchase price, holdback, contingency payment obligations or similar obligations, in each case, incurred or assumed in connection with the disposition or acquisition of any business, assets or Capital Stock of the Guarantors or any of their Subsidiaries;

(m) Indebtedness of the Guarantors or any of their Subsidiaries in respect of netting services, overdraft protection and otherwise in connection with deposit accounts, in each case, incurred in the ordinary course of business;

(n) Indebtedness representing deferred compensation to employees of the Guarantors or any of their Subsidiaries incurred in the ordinary course of business;

(o) Indebtedness incurred as a result of endorsing negotiable instruments received in the ordinary course of business by the Guarantors or any one of their Subsidiaries;

(p) Indebtedness incurred by the Guarantors or one of their Subsidiaries under customs bonds incurred in the ordinary course of business, to secure payments of customs duties in connection with the importation of goods that are promptly paid before they become due;

(q) [reserved]; and

(r) replacements, restatements, refundings, refinancings, amendments, supplements, modifications, extensions or renewals of any items of Permitted Indebtedness in paragraphs (a) and (c) through (k) above.

"**Person**" means an individual, a corporation, a company, a limited liability company, an association, a partnership, a joint venture, a joint stock company, a trust, an unincorporated organization, or a government or an agency or a political subdivision thereof.

"**Pfizer License**" means that License Agreement, by and among Iterum, the Irish Guarantor and Pfizer Inc., dated as of November 18, 2015, as it may be amended or otherwise modified from time to time.

"**Physical Notes**" means permanent certificated Notes in registered form issued in minimum denominations of $1,000 principal amount and multiples of $1,000 in excess thereof.

"**Physical Settlement**" shall have the meaning specified in Section 14.02(a).

"**Predecessor Note**" of any particular Note means every previous Note evidencing all or a portion of the same debt as that evidenced by such particular Note; and, for the purposes of this definition, any Note authenticated and delivered under Section 2.06 in lieu of or in exchange for a mutilated, lost, destroyed or stolen Note shall be deemed to evidence the same debt as the mutilated, lost, destroyed or stolen Note that it replaces.

"**Products**" means the Oral Product and the IV Product and "Product" means any one of them.

"**Record Date** " means, with respect to any dividend, distribution or other transaction or event in which the holders of Ordinary Shares (or other applicable security) have the right to receive any cash, securities or other property or in which the Ordinary Shares (or such other security) are exchanged for or converted into any combination of cash, securities or other property, the date fixed for determination of holders of the Ordinary Shares (or such other security) entitled to receive such cash, securities or other property (whether such date is fixed by Iterum's Board of Directors, by statute, by contract or otherwise).

"**Redemption Date**" shall have the meaning specified in Section 16.02(a).

"**Redemption Notice**" shall have the meaning specified in Section 16.02(a).

"**Redemption Payment Trigger Event**" means the first date on which both (i) Iterum (or Affiliate thereof) has received approval of a new drug application and, if applicable, a supplemental new drug application (or, in each case, any successor form or application having substantially the same effect with respect to the approval of a drug for marketing and sale) by the U.S. Food and Drug Administration with respect to a Product for the treatment of uncomplicated urinary tract infection and/or complicated urinary tract infection and (ii) there has been a commercial sale of a Product in the United States following approval by the U.S. Food and Drug Administration as provided in clause (i) above.

"**Redemption Price**" means, for any Notes to be redeemed pursuant to Section 16.01, (i) 300% of the outstanding principal amount of such Notes if the Redemption Date occurs prior to the Redemption Payment Trigger Event, (ii) 115% of the outstanding principal amount of such Notes if the Redemption Date occurs on or after the Redemption Payment Trigger Event or (iii)

notwithstanding clause (ii), if a Change of Control Transaction is consummated prior to or within 120 days after the applicable Redemption Date, the Change of Control Price, *plus*, in the case of each of clauses (i)-(iii), accrued and unpaid interest on such Notes to be redeemed, if any, to, but excluding, the Redemption Date (unless the Redemption Date falls after the Interest Record Date but on or prior to the Interest Payment Date, in which case interest accrued to the Interest Payment Date will be paid to Holders of record of such Notes as of the close of business on such Interest Record Date).

"**Reference Property**" shall have the meaning specified in Section 14.07(a).

"**Resale Restriction Termination Date**" shall have the meaning specified in Section 2.05(c).

"**Responsible Officer**," when used with respect to the Trustee, means any officer within the Corporate Trust Office of the Trustee to whom any corporate trust matter is referred because of such person's knowledge of and familiarity with the particular subject, and, in each case, who shall have direct responsibility for the administration of this Indenture.

"**Restricted Actions**" shall have the meaning specified in Section 4.11.

"**Restricted Securities**" shall have the meaning specified in Section 2.05(c).

"**Rights Offering**" means any public offering of subscription rights to purchase units consisting of Notes and RLNs by Iterum and the Company to holders of Ordinary Shares on a pro rata basis in accordance with their share ownership as of a record date to be determined by the Board of Directors of Iterum or a committee thereof. The Initial Purchasers and their Affiliates shall not be entitled to purchase any units pursuant to the Rights Offering (regardless of whether or not under Irish or other applicable law such subscription rights are required to be offered to the Initial Purchasers).

"**RLNs**" means the Limited Recourse Royalty-Linked Subordinated Notes issued by the Company pursuant to the RLN Indenture.

"**RLN Indenture**" means the Limited Recourse Royalty-Linked Subordinated Notes Indenture, dated as of January 21, 2020, by and among the Company, Iterum, the Subsidiary Guarantors, Iterum Holders' Representative LLC, as holders' representative, and Computershare Trust Company, N.A., as trustee.

"**Rule 144**" means Rule 144 as promulgated under the Securities Act.

"**Rule 144A**" means Rule 144A as promulgated under the Securities Act.

"**Scheduled Trading Day**" means a day that is scheduled to be a Trading Day on the principal U.S. national or regional securities exchange or market on which the Ordinary Shares are listed or admitted for trading. If the Ordinary Shares are not so listed or admitted for trading, "**Scheduled Trading Day**" means a Business Day.

"**Securities Act**" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"**Senior Debt**" means all obligations of the Company to Silicon Valley Bank now existing or hereafter arising, including, without limitation, (i) the Obligations (as defined in the SVB Facility), together with all costs of collecting such obligations (including attorneys' fees), (ii) all obligations now existing or hereafter arising under any agreement in connection with the provision by Silicon Valley Bank to the Company of products and/or credit services facilities, including, without limitation, any letters of credit, cash management services (including, without limitation, merchant services, direct deposit of payroll, business credit cards, and check cashing services), interest rate swap arrangements, and foreign exchange services, (iii) all interest accruing after the commencement by or against the Company of any bankruptcy, reorganization or similar proceeding, whether or not a claim for post-petition interest is allowed as a claim in the proceeding and (iv) any obligations of the Company hereafter arising that Iterum designates as "Senior Debt"; provided, however, that the aggregate principal amount of any such indebtedness shall not exceed $50,000,000 outstanding at any time (it being understood that the maximum amount of Senior Debt is not additive to the maximum amount of Guarantor Senior Debt but instead refers to the same maximum amount as applied to the Company with respect to Senior Debt and to each Guarantor with respect to Guarantor Senior Debt).

"**Settlement Amount**" shall have the meaning specified in Section 14.02(a)(iv).

"**Settlement Method**" means, with respect to any exchange of Notes, Physical Settlement, Cash Settlement or Combination Settlement, as elected (or deemed to have been elected) by the Company.

"**Settlement Notice**" shall have the meaning specified in Section 14.02(a)(iii).

"**Shareholder Approval**" means such approval as may be required from time to time by the applicable rules and regulations of the Nasdaq Stock Market (or any successor entity) from Iterum's shareholders with respect to the initial issuance of the Specified Notes to the Initial Purchasers and/or to permit the issuance of all Ordinary Shares issuable in connection with the exchange of all Specified Notes issued to the Initial Purchasers.

"**Significant Shareholder**" means any shareholder of Iterum that beneficially owns, directly or through its Affiliates and any other Persons or entities whose beneficial ownership of Ordinary Shares would be aggregated with such shareholder's beneficial ownership for purposes of Section 13(d) of the Exchange Act (excluding shares beneficially owned by virtue of the

ownership of securities or rights to acquire securities that have limitations on the right to exchange, convert, exercise or purchase similar to the limitation set forth herein), greater than 10% of the total number of Ordinary Shares issued and outstanding.

"**Significant Subsidiary**" means a Subsidiary of Iterum that meets the definition of "significant subsidiary" in Article 1, Rule 1-02 of Regulation S-X under the Exchange Act.

"**Special Interest**" means all amounts, if any, payable pursuant to Section 6.03.

"**Specified Dollar Amount**" means the maximum cash amount to be received upon exchange per $1,000 of principal of and accrued but unpaid interest on the Notes to be exchanged as determined by the Company and specified in the Settlement Notice related to any exchanged Notes.

"**Specified Notes**" means all the Notes originally issued to the Initial Purchasers on the date of this Indenture.

"**Specified Percentage**" means Sixty Six and Two Third Percent (66 2/3%); provided, however, that if greater than 50% of the initial aggregate principal of all Specified Notes (immediately following their original issuance) has been exchanged pursuant to Article 14, "**Specified Percentage**" shall mean Fifty Percent (50%).

"**Specified Transaction**" shall have the meaning specified in Section 14.07(a).

"**Spin-Off**" shall have the meaning specified in Section 14.04(c).

"**Subordinated Indebtedness**" means with respect to a Person, any Indebtedness of such Person that (i) is unsecured, (ii) is subordinated in right of payment to all principal and interest on the Notes or the Guarantee by such Person, as the case may be, pursuant to a written agreement to that effect and (iii) has no scheduled principal payment due on or before the Maturity Date.

"**Subsidiary**" means, with respect to any Person, any corporation, association, partnership or other business entity of which more than 50% of the total voting power of shares of Capital Stock or other interests (including partnership interests) entitled (without regard to the occurrence of any contingency) to vote in the election of directors, managers, general partners or trustees thereof is at the time owned or controlled, directly or indirectly, by (i) such Person; (ii) such Person and one or more Subsidiaries of such Person; or (iii) one or more Subsidiaries of such Person.

"**Subsidiary Guarantor**" shall have the meaning specified in the first paragraph of this Indenture.

"**Successor Company**" shall have the meaning specified in Section 11.01(a).

"**SVB Facility**" means that certain Loan and Security Agreement among the Subsidiary Guarantors, the Company and Silicon Valley Bank, dated as of April 27, 2018 (as may be amended, modified, restated, replaced, or supplemented from time to time, including any deferrals, renewals, refinancings or extensions thereof).

"**Trading Day**" means a day on which (i) trading in the Ordinary Shares (or other security for which a closing sale price must be determined) generally occurs on The Nasdaq Global Market or, if the Ordinary Shares (or such other security) are not then listed on The Nasdaq Global Market, on the principal other U.S. national or regional securities exchange on which the Ordinary Shares (or such other security) are then listed or, if the Ordinary Shares (or such other security) are not then listed on a U.S. national or regional securities exchange, on the principal other market on which the Ordinary Shares (or such other security) are then traded and (ii) a Last Reported Sale Price for the Ordinary Shares (or closing sale price for such other security) is available on such securities exchange or market; *provided* that if the Ordinary Shares (or such other security) are not so listed or traded, "**Trading Day**" means a Business Day; and *provided*, *further*, that for purposes of determining amounts due upon exchange only, "**Trading Day**" means a day on which (x) there is no Market Disruption Event and (y) trading in the Ordinary Shares generally occurs on The Nasdaq Global Market or, if the Ordinary Shares are not then listed on The Nasdaq Global Market, on the principal other U.S. national or regional securities exchange on which the Ordinary Shares are then listed or, if the Ordinary Shares are not then listed on a U.S. national or regional securities exchange, on the principal other market on which the Ordinary Shares are then listed or admitted for trading, except that if the Ordinary Shares are not so listed or admitted for trading, "**Trading Day**" means a Business Day.

"**transfer**" shall have the meaning specified in Section 2.05(c).

"**Trigger Event**" shall have the meaning specified in Section 14.04(c).

"**Trust Indenture Act**" means the U.S. Trust Indenture Act of 1939, as amended, as it was in force at the date of execution of this Indenture; *provided*, *however*, that in the event the Trust Indenture Act of 1939 is amended after the date hereof, the term "Trust Indenture Act" shall mean, to the extent required by such amendment, the Trust Indenture Act of 1939, as so amended.

"**Trustee**" means the Person named as the "**Trustee**" in the first paragraph of this Indenture until a successor trustee shall have become such pursuant to the applicable provisions of this Indenture, and thereafter "**Trustee**" shall mean or include each Person who is then a Trustee hereunder.

"**unit of Reference Property**" shall have the meaning specified in Section 14.07(a).

"**Unrestricted Cash**" means cash and/or Cash Equivalents that are free and clear of all liens, security interests or other charges or encumbrances and not subject to any restrictions on the use or distribution thereof to pay Indebtedness and other obligations or otherwise pursuant to applicable law or contract (other than any liens, security interests or other charges, encumbrances or restrictions pursuant to any Permitted Indebtedness described in clauses (a), (b), (f), (m), or (p) (or clause (r) to the extent related to clauses (a) or (f)) in the definition thereof).

"**Valuation Period**" shall have the meaning specified in Section 14.04(c).

"**Veto Notice**" shall have the meaning specified in Section 4.11.

Section 1.02 *References to Interest.* All references to interest on, or in respect of, any Note in this Indenture shall be deemed to include Special Interest if, in such context, Special Interest is, was or would be payable pursuant to Section 6.03 or to any interest payable on any Defaulted Amounts as set forth in Section 2.03(c).

Section 1.03 *Tax Treatment; OID.* The Company agrees and, by acceptance of a Note, each beneficial owner of a Note will be deemed to have agreed (a) to treat the Notes as indebtedness of the Company for U.S. federal income tax purposes, (b) that the Notes and RLNs constitute an "investment unit" for purposes of Section 1273(c)(2) of the Code, (c) that for purpose of the allocation of the issue price of such investment unit among the Notes and RLNs in accordance with Section 1273(c)(2) of the Code and the U.S. Department of the Treasury regulations Section 1.1273-2(h), $231.27 shall be allocated to the aggregate RLNs per investment unit, and (d) that neither the Company nor any beneficial owner shall take any position inconsistent with such allocation in any U.S. federal, state or local tax return unless otherwise required by a tax authority or court. Any Holder may obtain the amount of original issue discount for the Notes from the Company by submitting a written request to the Company at the following address: Iterum Therapeutics plc, Block 2, Floor 3 Harcourt Centre, Harcourt Street, Dublin 2, Ireland, Attention: Company Secretary.

ARTICLE 2
Issue, Description, Execution, Registration and Exchange of Notes

Section 2.01 *Designation and Amount.* The Notes shall be designated as the "6.500% Exchangeable Senior Subordinated Notes due 2025." The aggregate principal amount of Notes that may be authenticated and delivered under this Indenture is limited to $60,000,000 (inclusive of any additional Notes as contemplated by Section 2.10) (the "**Cap**") and except for Notes authenticated and delivered upon registration or transfer of, or in exchange for, or in lieu of other Notes pursuant to Section 2.05, Section 2.06, Section 2.07, Section 10.04, Section 14.02 and Section 15.04.

Section 2.02 *Form of Notes.* The Notes and the Trustee's certificate of authentication to be borne by such Notes shall be substantially in the respective forms set forth in Exhibit A, the

terms and provisions of which shall constitute, and are hereby expressly incorporated in and made a part of this Indenture. To the extent applicable, the Company, the Guarantors and the Trustee, by their execution and delivery of this Indenture, expressly agree to such terms and provisions and to be bound thereby.

Any Global Note may be endorsed with or have incorporated in the text thereof such legends or recitals or changes not inconsistent with the provisions of this Indenture as may be required by the Custodian or the Depositary, or as may be required to comply with any applicable law or any regulation thereunder or with the rules and regulations of any securities exchange or automated quotation system upon which the Notes may be listed or traded or designated for issuance or to conform with any usage with respect thereto, or to indicate any special limitations or restrictions to which any particular Notes are subject.

Any of the Notes may have such letters, numbers or other marks of identification and such notations, legends or endorsements as the Officers executing the same may approve (execution thereof to be conclusive evidence of such approval) and as are not inconsistent with the provisions of this Indenture, or as may be required to comply with any law or with any rule or regulation made pursuant thereto or with any rule or regulation of any securities exchange or automated quotation system on which the Notes may be listed or designated for issuance, or to conform to usage or to indicate any special limitations or restrictions to which any particular Notes are subject.

Each Global Note shall represent such principal amount of the outstanding Notes as shall be specified therein and shall provide that it shall represent the aggregate principal amount of outstanding Notes from time to time endorsed thereon and that the aggregate principal amount of outstanding Notes represented thereby may from time to time be increased or reduced to reflect redemptions, repurchases, cancellations, exchanges for cash, Ordinary Shares or a combination thereof, transfers or exchanges permitted hereby. Any endorsement of a Global Note to reflect the amount of any increase or decrease in the amount of outstanding Notes represented thereby shall be made by the Trustee or the Custodian, at the direction of the Trustee, in such manner and upon instructions given by the Company or the Holder of such Notes in accordance with this Indenture. Payment of principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, and any accrued and unpaid interest on, a Global Note shall be made to the Holder of such Note on the date of payment, unless a record date or other means of determining Holders eligible to receive payment is provided for herein.

Section 2.03 *Date and Denomination of Notes; Payments of Interest and Defaulted Amounts.* (a) The Notes shall be issuable in registered form without coupons in minimum denominations of $1,000 principal amount and multiples of $1,000 in excess thereof. Each Note shall be dated the date of its authentication and shall bear simple, non-compounding interest from the date specified on the face of such Note to, but excluding, the Maturity Date, unless earlier repurchased, redeemed or exchanged pursuant to and in accordance with the provisions of

this Indenture. Accrued interest on the Notes, if any, shall be computed on the basis of a 360-day year composed of twelve 30-day months and, for partial months, on the basis of actual days elapsed over a 30-day month.

(b) The Person in whose name any Note (or its Predecessor Note) is registered on the Note Register at the close of business on the Interest Record Date with respect to the Interest Payment Date shall be entitled to receive any interest payable on the Interest Payment Date. The principal amount of any Note (x) in the case of any Physical Note, shall be payable at the office or agency of the Company maintained by the Company for such purposes in the United States of America, which shall initially be the Corporate Trust Office and (y) in the case of any Global Note, shall be payable by wire transfer of immediately available funds to the account of the Depositary or its nominee. The Company shall pay interest, if any, (i) on any Physical Notes (a) to Holders holding Physical Notes having an aggregate principal amount of $5,000,000 or less, by check delivered to the Holders of these Notes at their address as it appears in the Note Register and (b) to Holders holding Physical Notes having an aggregate principal amount of more than $5,000,000, either by check delivered to each such Holder or, upon application by such a Holder to the Note Registrar not later than the relevant Interest Record Date, by wire transfer in immediately available funds to that Holder's account within the United States, which application shall remain in effect until the Holder notifies, in writing, the Note Registrar to the contrary or (ii) on any Global Note by wire transfer of immediately available funds to the account of the Depositary or its nominee.

(c) Any Defaulted Amounts shall forthwith cease to be payable to the Holder on the relevant payment date but shall accrue interest, to the extent permitted by applicable law, per annum at the rate borne by the Notes, from, and including, such relevant payment date, and such Defaulted Amounts together with any such interest thereon shall be paid by the Company, at its election in each case, as provided in clause (i) or (ii) below:

(i) The Company may elect to make payment of any Defaulted Amounts to the Persons in whose names the Notes (or their respective Predecessor Notes) are registered at the close of business on a special record date for the payment of such Defaulted Amounts, which shall be fixed in the following manner. The Company shall notify the Trustee in writing of the amount of the Defaulted Amounts proposed to be paid on each Note and the date of the proposed payment (which shall be not less than 25 days after the receipt by the Trustee of such notice, unless the Trustee shall consent to an earlier date), and at the same time the Company shall deposit with the Trustee an amount of money equal to the aggregate amount to be paid in respect of such Defaulted Amounts or shall make arrangements satisfactory to the Trustee for such deposit on or prior to the date of the proposed payment, such money when deposited to be held in trust for the benefit of the Persons entitled to such Defaulted Amounts as in this clause provided. Thereupon the Company shall fix a special record date for the payment of such Defaulted Amounts which shall be not more than 15 days and not less than 10 days prior to the date

of the proposed payment, and not less than 10 days after the receipt by the Trustee of the notice of the proposed payment. The Company shall promptly notify the Trustee in writing of such special record date and the Trustee, in the name and at the expense of the Company, shall cause notice of the proposed payment of such Defaulted Amounts and the special record date therefor to be delivered to each Holder at its address as it appears in the Note Register, or by electronic means to the Depositary in the case of Global Notes, not less than 10 days prior to such special record date. Notice of the proposed payment of such Defaulted Amounts and the special record date therefor having been so delivered, such Defaulted Amounts shall be paid to the Persons in whose names the Notes (or their respective Predecessor Notes) are registered at the close of business on such special record date and shall no longer be payable pursuant to the following clause (ii) of this Section 2.03(c).

(ii) The Company may make payment of any Defaulted Amounts in any other lawful manner not inconsistent with the requirements of any securities exchange or automated quotation system on which the Notes may be listed or designated for issuance, and upon such notice as may be required by such exchange or automated quotation system, if, after written notice given by the Company to the Trustee of the proposed payment pursuant to this clause, such manner of payment shall be deemed practicable by the Trustee.

Section 2.04 *Execution, Authentication and Delivery of Notes.* The Notes shall be signed in the name and on behalf of the Company by the manual or facsimile signature of an Officer of the Company.

At any time and from time to time after the execution and delivery of this Indenture, the Company may deliver Notes executed by the Company to the Trustee for authentication, together with a Company Order for the authentication and delivery of such Notes, and the Trustee in accordance with such Company Order shall authenticate and deliver such Notes, without any further action by the Company hereunder, other than delivery of an Officer's Certificate pursuant to Section 17.05. For the avoidance of doubt, the Trustee shall not be obligated to authenticate a Note hereunder unless and until it has received a Company Order in accordance with the terms hereof.

Only such Notes as shall bear thereon a certificate of authentication substantially in the form set forth on the form of Note attached as Exhibit A hereto, executed manually by an authorized signatory of the Trustee (or an authenticating agent appointed by the Trustee as provided by Section 17.10), shall be entitled to the benefits of this Indenture or be valid or obligatory for any purpose. Such certificate by the Trustee (or such an authenticating agent) upon any Note executed by the Company shall be conclusive evidence that the Note so authenticated has been duly authenticated and delivered hereunder and that the Holder is entitled to the benefits of this Indenture.

In case any Officer of the Company who shall have signed any of the Notes shall cease to be such Officer before the Notes so signed shall have been authenticated and delivered by the Trustee, or disposed of by the Company, such Notes nevertheless may be authenticated and delivered or disposed of as though the Person who signed such Notes had not ceased to be such Officer of the Company; and any Note may be signed on behalf of the Company by such persons as, at the actual date of the execution of such Note, shall be the Officers of the Company, although at the date of the execution of this Indenture any such Person was not such an Officer.

Section 2.05 *Exchange and Registration of Transfer of Notes; Restrictions on Transfer; Depositary.* (a) The Company shall cause to be kept at the Corporate Trust Office a register (the register maintained in such office or in any other office or agency of the Company designated pursuant to Section 4.02, the "**Note Register**") in which, subject to such reasonable regulations as it may prescribe, the Company shall provide for the registration of Notes and of transfers of Notes. Such register shall be in written form or in any form capable of being converted into written form within a reasonable period of time. The Trustee is hereby initially appointed the "**Note Registrar**" for the purpose of registering Notes and transfers of Notes as herein provided. The Company may appoint one or more co-Note Registrars in accordance with Section 4.02.

Upon surrender for registration of transfer of any Note to the Note Registrar or any co-Note Registrar, and satisfaction of the requirements for such transfer set forth in this Section 2.05, the Company shall execute, and upon receipt of a Company Order, the Trustee shall authenticate and deliver, in the name of the designated transferee or transferees, one or more new Notes of any authorized denominations and of a like aggregate principal amount and bearing such restrictive legends as may be required by this Indenture.

Notes may be exchanged for other Notes of any authorized denominations and of a like aggregate principal amount, upon surrender of the Notes to be exchanged at any such office or agency maintained by the Company pursuant to Section 4.02. Whenever any Notes are so surrendered for exchange, the Company shall execute, and upon receipt of a Company Order, the Trustee shall authenticate and deliver, the Notes that the Holder making the exchange is entitled to receive, bearing registration numbers not contemporaneously outstanding.

All Notes presented or surrendered for registration of transfer or for exchange, repurchase or exchanges for cash, Ordinary Shares or a combination thereof shall (if so required by the Company, the Trustee, the Note Registrar or any co-Note Registrar) be duly endorsed, or be accompanied by a written instrument or instruments of transfer in form satisfactory to the Note Registrar and the Company and duly executed, by the Holder thereof or its attorney-in-fact duly authorized in writing.

No service charge shall be imposed by the Company, the Trustee, the Note Registrar, any co-Note Registrar or the Paying Agent for any exchange or registration of transfer of Notes, but the Trustee, the Note Registrar or the Company may require a Holder to pay a sum sufficient to

cover any documentary, stamp or similar issue or transfer tax required in connection therewith as a result of the name of the Holder of new Notes issued upon such exchange or registration of transfer being different from the name of the Holder of the old Notes surrendered for exchange or registration of transfer.

None of the Company, the Trustee, the Note Registrar or any co-Note Registrar shall be required to exchange or register a transfer of (i) any Notes surrendered for exchanges for cash, Ordinary Shares or a combination thereof or, if a portion of any Note is surrendered for exchanges for cash, Ordinary Shares or a combination thereof, such portion thereof surrendered for exchanges for cash, Ordinary Shares or a combination thereof, (ii) any Notes, or a portion of any Note, surrendered for repurchase (and not withdrawn) in accordance with Article 15 or (iii) any Notes selected for redemption in accordance with Article 16, except the unredeemed portion of any Note being redeemed in part.

All Notes issued upon any registration of transfer or exchange of Notes in accordance with this Indenture shall be the valid obligations of the Company, evidencing the same debt, and entitled to the same benefits under this Indenture as the Notes surrendered upon such registration of transfer or exchange.

(b) The Specified Notes issued hereunder shall be represented initially by Physical Notes until such time as the Shareholder Approval has been obtained. Otherwise, so long as the Notes are eligible for book-entry settlement with the Depositary, unless otherwise required by law, subject to the fourth paragraph from the end of Section 2.05(c) all Notes issued under this Indenture shall be represented by one or more Notes in global form (each, a "**Global Note**") registered in the name of the Depositary or the nominee of the Depositary. The transfer and exchange of beneficial interests in a Global Note that does not involve the issuance of a Physical Note shall be effected through the Depositary (but not the Trustee or the Custodian) in accordance with this Indenture (including the restrictions on transfer set forth herein) and the procedures of the Depositary therefor.

(c) Every Note that bears or is required under this Section 2.05(c) to bear the legend set forth in this Section 2.05(c) (together with any Ordinary Shares issued upon exchange of the Notes that are required to bear the legend set forth in Section 2.05(d), collectively, the "**Restricted Securities**") shall be subject to the restrictions on transfer set forth in this Section 2.05(c) (including those contained in the legend set forth below), unless such restrictions on transfer shall be eliminated or otherwise waived by written consent of the Company, and the Holder of each such Restricted Security, by such Holder's acceptance thereof, agrees to be bound by all such restrictions on transfer. As used in this Section 2.05(c) and Section 2.05(d), the term "**transfer**" encompasses any sale, pledge, transfer or other disposition whatsoever of any Restricted Security. For the avoidance of doubt, nothing in this Section 2.05(c) shall be deemed to prevent the transfer of any Note by any Holder to any Affiliate of such Holder in a transaction that is otherwise in compliance with the Securities Act.

Until the date (the "**Resale Restriction Termination Date**") that is the later of (1) the date that is one year after the last date of original issuance of the Notes, or such shorter period of time as permitted by Rule 144 or any successor provision thereto, and (2) such later date, if any, as may be required by applicable law, including as a result of the affiliate status of any holder of a Note, any certificate evidencing such Note (and all securities issued in exchange therefor or substitution thereof, other than Ordinary Shares, if any, issued upon exchange thereof, which shall bear the legend set forth in Section 2.05(d), if applicable) shall bear a legend in substantially the following form (unless such Notes have been transferred pursuant to a registration statement that has become or been declared effective under the Securities Act and that was effective at the time of such transfer, or sold pursuant to the exemption from registration provided by Rule 144 or any similar provision then in force under the Securities Act, or unless otherwise agreed by the Company in writing, with notice thereof to the Trustee):

THIS SECURITY AND THE ORDINARY SHARES, IF ANY, DELIVERABLE UPON EXCHANGE OF THIS SECURITY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "**SECURITIES ACT**"), AND MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED EXCEPT IN ACCORDANCE WITH THE FOLLOWING SENTENCE. BY ITS ACQUISITION HEREOF OR OF A BENEFICIAL INTEREST HEREIN, THE ACQUIRER:

(1) REPRESENTS THAT IT AND ANY ACCOUNT FOR WHICH IT IS ACTING IS AN "ACCREDITED INVESTOR" (WITHIN THE MEANING OF RULE 501 UNDER THE SECURITIES ACT), THAT IT EXERCISES SOLE INVESTMENT DISCRETION WITH RESPECT TO EACH SUCH ACCOUNT, AND THAT IT AND ANY SUCH ACCOUNT IS NOT AN AFFILIATE OF ITERUM THERAPEUTICS BERMUDA LIMITED (THE "**COMPANY**"), ITERUM THERAPEUTICS PLC ("**ITERUM**"), ITERUM THERAPEUTICS INTERNATIONAL LIMITED (THE "**IRISH GUARANTOR**"), ITERUM THERAPEUTICS US LIMITED ("**ITERUM U.S. LIMITED**") OR ITERUM THERAPEUTICS US HOLDING LIMITED (TOGETHER WITH ITERUM, THE IRISH GUARANTOR AND ITERUM U.S. LIMITED, THE "**GUARANTORS**"), AND

(2) AGREES FOR THE BENEFIT OF THE COMPANY AND THE GUARANTORS THAT IT WILL NOT OFFER, SELL, PLEDGE OR OTHERWISE TRANSFER THIS SECURITY OR ANY BENEFICIAL INTEREST HEREIN PRIOR TO THE DATE THAT IS THE LATER OF (X) ONE YEAR AFTER THE LAST ORIGINAL ISSUE DATE HEREOF OR SUCH SHORTER PERIOD OF TIME AS PERMITTED BY RULE 144 UNDER THE SECURITIES ACT OR ANY SUCCESSOR PROVISION THERETO AND (Y) SUCH LATER DATE, IF ANY, AS MAY BE REQUIRED BY APPLICABLE LAW, EXCEPT:

(A) TO ITERUM OR ANY SUBSIDIARY THEREOF (INCLUDING THE COMPANY), OR

(B) PURSUANT TO A REGISTRATION STATEMENT WHICH HAS BECOME EFFECTIVE UNDER THE SECURITIES ACT, OR

(C) TO A QUALIFIED INSTITUTIONAL BUYER IN COMPLIANCE WITH RULE 144A UNDER THE SECURITIES ACT, OR

(D) PURSUANT TO AN EXEMPTION FROM REGISTRATION PROVIDED BY RULE 144 UNDER THE SECURITIES ACT OR ANY OTHER AVAILABLE EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

PRIOR TO THE REGISTRATION OF ANY TRANSFER IN ACCORDANCE WITH CLAUSE (2)(D) ABOVE, THE COMPANY, THE GUARANTORS AND THE TRUSTEE RESERVE THE RIGHT TO REQUIRE THE DELIVERY OF SUCH LEGAL OPINIONS, CERTIFICATIONS OR OTHER EVIDENCE AS MAY REASONABLY BE REQUIRED IN ORDER TO DETERMINE THAT THE PROPOSED TRANSFER IS BEING MADE IN COMPLIANCE WITH THE SECURITIES ACT AND APPLICABLE STATE SECURITIES LAWS. NO REPRESENTATION IS MADE AS TO THE AVAILABILITY OF ANY EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

THE HOLDER OF THIS SECURITY IS ENTITLED TO THE BENEFITS OF A INVESTOR RIGHTS AGREEMENT (AS SUCH TERM IS DEFINED IN THE INDENTURE REFERRED TO ON THE REVERSE HEREOF) AND, BY ITS ACCEPTANCE HEREOF, AGREES TO BE BOUND BY AND TO COMPLY WITH THE PROVISIONS OF SUCH INVESTOR RIGHTS AGREEMENT.

No transfer prior to the Resale Restriction Termination Date of any Note as to which such restrictions on transfer apply will be registered by the Note Registrar unless the applicable box on the Form of Assignment and Transfer has been checked.

Any Note (or security issued in exchange or substitution therefor) as to which such restrictions on transfer shall have expired in accordance with their terms may, upon surrender of such Note for exchange to the Note Registrar in accordance with the provisions of this Section 2.05, be exchanged for a new Note or Notes, of like tenor and aggregate principal amount, which shall not bear the restrictive legend required by this Section 2.05(c) and shall not be assigned a restricted CUSIP number. The Company shall be entitled to instruct the Custodian in writing to so surrender any Global Note as to which such restrictions on transfer shall have expired in accordance with their terms for exchange, and, upon such instruction, the Custodian shall so surrender such Global Note for exchange; and any new Global Note so exchanged therefor shall not bear the restrictive legend specified in this Section 2.05(c) and shall not be assigned a restricted CUSIP number. The Company shall promptly notify the Trustee in writing upon the occurrence of the Resale Restriction Termination Date and promptly after a registration

statement, if any, with respect to the Notes or any Ordinary Shares delivered upon exchange of the Notes has been declared effective under the Securities Act.

Notwithstanding any other provisions of this Indenture (other than the provisions set forth in this Section 2.05(c)), a Global Note may not be transferred as a whole or in part except (i) by the Depositary to a nominee of the Depositary or by a nominee of the Depositary to the Depositary or another nominee of the Depositary or by the Depositary or any such nominee to a successor Depositary or a nominee of such successor Depositary and (ii) for transfers of portions of a Global Note in certificated form made upon request of a member of, or a participant in, the Depositary (for itself or on behalf of a beneficial holder) by written notice given to the Trustee by or on behalf of the Depositary in accordance with customary procedures of the Depositary and in compliance with this Section 2.05(c).

The Depositary shall be a clearing agency registered under the Exchange Act. The Company initially appoints The Depository Trust Company to act as Depositary with respect to each Global Note. Initially, each Global Note shall be issued to the Depositary, registered in the name of Cede & Co., as the nominee of the Depositary, and deposited with the Trustee as custodian for Cede & Co.

Only if (i) the Depositary notifies the Company at any time that the Depositary is unwilling or unable to continue as depositary for the Global Notes and a successor depositary is not appointed within 90 days, (ii) the Depositary ceases to be registered as a clearing agency under the Exchange Act and a successor depositary is not appointed within 90 days, (iii) a Beneficial Holder notifies the Company that it is an Affiliate of the Company or the Parent Guarantor and requests that its beneficial interest in the Global Note be issued as a Physical Note, or (iv) an Event of Default with respect to the Notes has occurred and is continuing, or a Mandatory Exchange Notice has been delivered, and a beneficial holder of an interest in any Global Note (a "**Beneficial Holder**") requests that its beneficial interest therein be issued as a Physical Note, the Company shall execute, and the Trustee, upon receipt of an Officer's Certificate and a Company Order for the authentication and delivery of Notes, shall authenticate and deliver at the Company's expense (x) in the case of clause (iii) or (iv), a Physical Note to such Beneficial Holder in a principal amount equal to the principal amount of such Note corresponding such Beneficial Holder's beneficial interest and (y) in the case of clause (i) or (ii), Physical Notes to each Beneficial Holder of the related Global Notes (or a portion thereof) in an aggregate principal amount equal to the aggregate principal amount of such Global Notes in exchange for such Global Notes, and upon delivery of the Global Notes to the Trustee such Global Notes shall be canceled.

Physical Notes issued in exchange for all or a part of the Global Note pursuant to this Section 2.05(c) shall be registered in such names and in such authorized denominations as the Depositary, pursuant to instructions from its direct or indirect participants or otherwise, or, in the case of clause (iii) or (iv) of the immediately preceding paragraph, the relevant Beneficial

Holder, shall instruct the Trustee in writing. Upon execution and authentication, the Trustee shall deliver at the Company's expense such Physical Notes to the Persons in whose names such Physical Notes are so registered.

At such time as all interests in a Global Note have been exchanged for cash, Ordinary Shares or a combination thereof, canceled, repurchased, redeemed or transferred, such Global Note shall be, upon receipt thereof, canceled by the Trustee in accordance with standing procedures and existing instructions between the Depositary and the Custodian. At any time prior to such cancellation, if any interest in a Global Note is exchanged for Physical Notes, exchanged for cash, Ordinary Shares or a combination thereof, canceled, redeemed, repurchased or transferred to a transferee who receives Physical Notes therefor or any Physical Note is exchanged, redeemed, repurchased or transferred for part of such Global Note, the principal amount of such Global Note shall, in accordance with the standing procedures and instructions existing between the Depositary and the Custodian, be appropriately reduced or increased, as the case may be, and an endorsement shall be made on such Global Note, by the Trustee or the Custodian, at the direction of the Trustee, to reflect such reduction or increase.

None of the Company, the Guarantors, the Trustee or any agent of the Company, the Guarantors or the Trustee shall have any responsibility or liability to any Beneficial Holder of a Global Note, a member of, or a participant in, the Depositary or other Person for any aspect of the records relating to or payments made on account of beneficial ownership interests of a Global Note or maintaining, supervising or reviewing any records relating to such beneficial ownership interests.

(d) Until the Resale Restriction Termination Date, any stock certificate representing Ordinary Shares delivered upon exchange of Notes to which restrictions on transfer apply shall bear a legend in substantially the following form (unless such Ordinary Shares have been transferred pursuant to a registration statement that has become or been declared effective under the Securities Act and that was effective at the time of such transfer, or pursuant to the exemption from registration provided by Rule 144 or any similar provision then in force under the Securities Act, or such Ordinary Shares have been delivered upon exchange of a Note that has been transferred pursuant to a registration statement that has become or been declared effective under the Securities Act and that was effective at the time of such transfer, or pursuant to the exemption from registration provided by Rule 144 or any similar provision then in force under the Securities Act, or unless otherwise agreed by the Company with written notice thereof to the Trustee and any transfer agent for the Ordinary Shares):

THIS SECURITY HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "**SECURITIES ACT**"), AND MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED EXCEPT IN ACCORDANCE WITH THE FOLLOWING SENTENCE. BY ITS ACQUISITION HEREOF OR OF A BENEFICIAL INTEREST HEREIN, THE ACQUIRER:

(1) REPRESENTS THAT IT AND ANY ACCOUNT FOR WHICH IT IS ACTING IS AN "ACCREDITED INVESTOR" (WITHIN THE MEANING OF RULE 501 UNDER THE SECURITIES ACT), THAT IT EXERCISES SOLE INVESTMENT DISCRETION WITH RESPECT TO EACH SUCH ACCOUNT AND THAT IT AND ANY SUCH ACCOUNT IS NOT AN AFFILIATE OF ITERUM THERAPEUTICS BERMUDA LIMITED (THE "**COMPANY**"), ITERUM THERAPEUTICS PLC ("**ITERUM**"), ITERUM THERAPEUTICS INTERNATIONAL LIMITED (THE "**IRISH GUARANTOR**"), ITERUM THERAPEUTICS US LIMITED ("**ITERUM U.S. LIMITED**") OR ITERUM THERAPEUTICS US HOLDING LIMITED (TOGETHER WITH ITERUM, THE IRISH GUARANTOR AND ITERUM U.S. LIMITED, THE "**GUARANTORS**"), AND

(2) AGREES FOR THE BENEFIT OF THE COMPANY AND THE GUARANTORS THAT IT WILL NOT OFFER, SELL, PLEDGE OR OTHERWISE TRANSFER THIS SECURITY OR ANY BENEFICIAL INTEREST HEREIN PRIOR TO THE DATE THAT IS THE LATER OF (X) ONE YEAR AFTER THE LAST ORIGINAL ISSUE DATE OF THE SERIES OF NOTES UPON THE EXCHANGE OF WHICH THIS SECURITY WAS ISSUED OR SUCH SHORTER PERIOD OF TIME AS PERMITTED BY RULE 144 UNDER THE SECURITIES ACT OR ANY SUCCESSOR PROVISION THERETO AND (Y) SUCH LATER DATE, IF ANY, AS MAY BE REQUIRED BY APPLICABLE LAW, EXCEPT:

(A) TO ITERUM OR ANY SUBSIDIARY THEREOF (INCLUDING THE COMPANY), OR

(B) PURSUANT TO A REGISTRATION STATEMENT WHICH HAS BECOME EFFECTIVE UNDER THE SECURITIES ACT, OR

(C) TO A QUALIFIED INSTITUTIONAL BUYER IN COMPLIANCE WITH RULE 144A UNDER THE SECURITIES ACT, OR

(D) PURSUANT TO AN EXEMPTION FROM REGISTRATION PROVIDED BY RULE 144 UNDER THE SECURITIES ACT OR ANY OTHER AVAILABLE EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

PRIOR TO THE REGISTRATION OF ANY TRANSFER IN ACCORDANCE WITH CLAUSE (2)(D) ABOVE, THE COMPANY, THE GUARANTORS AND THE TRANSFER AGENT FOR THE COMPANY'S ORDINARY SHARES RESERVE THE RIGHT TO REQUIRE THE DELIVERY OF SUCH LEGAL OPINIONS, CERTIFICATIONS OR OTHER EVIDENCE AS MAY REASONABLY BE REQUIRED IN ORDER TO DETERMINE THAT THE PROPOSED TRANSFER IS BEING MADE IN COMPLIANCE WITH THE SECURITIES ACT AND APPLICABLE STATE SECURITIES LAWS. NO REPRESENTATION IS MADE AS TO THE AVAILABILITY OF ANY EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

THE HOLDER OF THIS SECURITY IS ENTITLED TO THE BENEFITS OF A INVESTOR RIGHTS AGREEMENT (AS SUCH TERM IS DEFINED IN THE INDENTURE REFERRED TO ON THE REVERSE HEREOF) AND, BY ITS ACCEPTANCE HEREOF, AGREES TO BE BOUND BY AND TO COMPLY WITH THE PROVISIONS OF SUCH INVESTOR RIGHTS AGREEMENT.

Any such Ordinary Shares as to which such restrictions on transfer shall have expired in accordance with their terms may, upon surrender of the certificates representing such Ordinary Shares for exchange in accordance with the procedures of the transfer agent for the Ordinary Shares, be exchanged for a new certificate or certificates for a like aggregate number of Ordinary Shares, which shall not bear the restrictive legend required by this Section 2.05(d).

(e) Notwithstanding anything contained herein to the contrary, neither the Trustee nor the Note Registrar shall be responsible for ascertaining whether any transfer complies with the registration provisions of, or exemptions from, the Securities Act, applicable state securities laws or other applicable law.

(f) Any Note or Ordinary Shares issued upon the exchange of a Note that is repurchased or owned by any Affiliate of the Company or Iterum (or any Person who was an Affiliate of the Company or Iterum at any time during the three months immediately preceding) may not be resold by such Affiliate (or such Person, as the case may be) unless registered under the Securities Act or resold pursuant to an exemption from the registration requirements of the Securities Act in a transaction that results in such Note or Ordinary Shares, as the case may be, no longer being a "restricted security" (as defined under Rule 144). Except as provided for in Section 2.10, each of the Company and Iterum shall cause any Note that is repurchased or owned by it to be surrendered to the Trustee for cancellation in accordance with Section 2.08.

(g) The Trustee shall have no obligation or duty to monitor, determine or inquire as to compliance with any restrictions on transfer imposed under this Indenture or under applicable law with respect to any transfer of any interest in any Note (including any transfers between or among depositary participants or Beneficial Holders of interests in any Global Note) other than to require delivery of such certificates and other documentation or evidence as are expressly required by, and to do so if and when expressly required by the terms of, this Indenture, and to examine the same to determine substantial compliance as to form with the express requirements hereof.

(h) Neither the Trustee nor any agent shall have any responsibility or liability for any actions or omissions taken or not taken by the Depositary. All notices and communications to be given to the Holders and all payments to be made to the Holders in respect of the Notes shall be given or made only to, or upon the order of, the registered Holder(s) (which shall be the Depositary or its nominee in the case of a Global Note). The rights of Beneficial Holders in any Global Note shall be exercised only through the Depositary subject to the applicable procedures

of the Depositary. The Trustee may rely and shall be fully protected in relying upon information furnished by the Depositary with respect to its members, participants and any Beneficial Holders.

Section 2.06 *Mutilated, Destroyed, Lost or Stolen Notes.* In case any Note shall become mutilated or be destroyed, lost or stolen, the Company in its discretion may execute, and upon receipt of a Company Order the Trustee or an authenticating agent appointed by the Trustee shall authenticate and deliver, a new Note, bearing a registration number not contemporaneously outstanding, in exchange and substitution for the mutilated Note, or in lieu of and in substitution for the Note so destroyed, lost or stolen. In every case the applicant for a substituted Note shall furnish to the Company, to the Trustee and, if applicable, to such authenticating agent such security and/or indemnity satisfactory to the Company, the Trustee, or if applicable, the authenticating agent as may be required by them to save each of them harmless from any loss, liability, cost or expense caused by or connected with such substitution, and, in every case of destruction, loss or theft, the applicant shall also furnish to the Company, to the Trustee and, if applicable, to such authenticating agent evidence to their satisfaction of the destruction, loss or theft of such Note and of the ownership thereof.

The Trustee or such authenticating agent may authenticate any such substituted Note and deliver the same upon the receipt of such security and/or indemnity as the Trustee, the Company and, if applicable, such authenticating agent may require. No service charge shall be imposed by the Company, the Trustee, the Note Registrar, any co-Note Registrar or the Paying Agent upon the issuance of any substitute Note, but the Company and/or the Trustee may require a Holder to pay a sum sufficient to cover any documentary, stamp or similar issue or transfer tax required in connection therewith as a result of the name of the Holder of the new substitute Note being different from the name of the Holder of the old Note that became mutilated or was destroyed, lost or stolen. In case any Note that has matured or is about to mature or has been surrendered for required repurchase or redemption or is about to be exchanged in accordance with Article 14 shall become mutilated or be destroyed, lost or stolen, the Company may, in its sole discretion, instead of issuing a substitute Note, pay or authorize the payment of or exchange or authorize the exchange of the same (without surrender thereof except in the case of a mutilated Note), as the case may be, if the applicant for such payment or exchange shall furnish to the Company, to the Trustee and, if applicable, to such authenticating agent such security and/or indemnity as may be required by them to save each of them harmless for any loss, liability, cost or expense caused by or connected with such substitution, and, in every case of destruction, loss or theft, evidence satisfactory to the Company, the Trustee and, if applicable, any Paying Agent or Exchange Agent of the destruction, loss or theft of such Note and of the ownership thereof.

Every substitute Note issued pursuant to the provisions of this Section 2.06 by virtue of the fact that any Note is destroyed, lost or stolen shall constitute an additional contractual obligation of the Company, whether or not the destroyed, lost or stolen Note shall be found at any time, and shall be entitled to all the benefits of (but shall be subject to all the limitations set forth in) this Indenture equally and proportionately with any and all other Notes duly issued

hereunder. To the extent permitted by law, all Notes shall be held and owned upon the express condition that the foregoing provisions are exclusive with respect to the replacement, payment, redemption, exchange or repurchase of mutilated, destroyed, lost or stolen Notes and shall preclude any and all other rights or remedies notwithstanding any law or statute existing or hereafter enacted to the contrary with respect to the replacement, payment, redemption, exchange or repurchase of negotiable instruments or other securities without their surrender.

Section 2.07 *Temporary Notes.* Pending the preparation of Physical Notes, the Company may execute and the Trustee or an authenticating agent appointed by the Trustee shall, upon written request of the Company, authenticate and deliver temporary Notes (printed or lithographed). Temporary Notes shall be issuable in any authorized denomination, and substantially in the form of the Physical Notes but with such omissions, insertions and variations as may be appropriate for temporary Notes, all as may be determined by the Company. Every such temporary Note shall be executed by the Company and authenticated by the Trustee or such authenticating agent upon the same conditions and in substantially the same manner, and with the same effect, as the Physical Notes. Without unreasonable delay, the Company shall execute and deliver to the Trustee or such authenticating agent Physical Notes (other than any Global Note) and thereupon any or all temporary Notes (other than any Global Note) may be surrendered in exchange therefor, at each office or agency maintained by the Company pursuant to Section 4.02 and the Trustee or such authenticating agent shall authenticate and deliver in exchange for such temporary Notes an equal aggregate principal amount of Physical Notes. Such exchange shall be made by the Company at its own expense and without any charge therefor. Until so exchanged, the temporary Notes shall in all respects be entitled to the same benefits and subject to the same limitations under this Indenture as Physical Notes authenticated and delivered hereunder.

Section 2.08 *Cancellation of Notes Paid, Exchanged, Etc.* The Company shall cause all Notes surrendered for the purpose of payment, redemption, repurchase, exchange for cash, Ordinary Shares or a combination thereof, or registration of transfer or exchange, if surrendered to any Person other than the Trustee (including any of the Company's agents or the Guarantors' or the Company's respective Subsidiaries or Affiliates), to be surrendered to the Trustee for cancellation. All Notes delivered to the Trustee shall be canceled promptly by it, and no Notes shall be authenticated in exchange therefor except as expressly permitted by any of the provisions of this Indenture. The Trustee shall dispose of canceled Notes in accordance with its customary procedures and, after such disposition, shall deliver evidence of such disposition to the Company, at the Company's written request in a Company Order.

Section 2.09 *CUSIP and ISIN Numbers.* The Company in issuing the Notes may use "CUSIP" and/or "ISIN" numbers (if then generally in use), and, if so, the Trustee shall use "CUSIP" and/or "ISIN" numbers in all notices issued to Holders as a convenience to such Holders; *provided* that any such notice may state that no representation is made as to the correctness of such numbers either as printed on the Notes or on such notice and that reliance

may be placed only on the other identification numbers printed on the Notes. The Company shall promptly notify the Trustee in writing of any change in the "CUSIP" and/or "ISIN" numbers.

Section 2.10 *Additional Notes; Repurchases.* The Company may, without the consent of the Holders, but subject in all cases to the Cap, reopen this Indenture and issue additional Notes hereunder with the same terms as the Notes initially issued hereunder (except for the issue date, issue price and, in some cases, the initial interest accrual date); *provided* that if any such additional Notes are not fungible with the Notes initially issued hereunder for U.S. federal income tax and securities law purposes, such additional Notes shall have one or more separate CUSIP numbers. Prior to the issuance of any such additional Notes, the Company shall deliver to the Trustee a Company Order, an Officer's Certificate and an Opinion of Counsel, such Officer's Certificate and Opinion of Counsel to cover such matters applicable to the issuance of additional Notes, in addition to those required by Section 17.05. In addition, the Company and/or the Guarantors may, to the extent permitted by law, and directly or indirectly (regardless of whether such Notes are surrendered to the Company or the Guarantors), repurchase Notes in the open market or otherwise, whether by the Company, the Guarantors or their respective Subsidiaries or through a private or public tender or exchange offer or through counterparties to private agreements, including by cash-settled swaps or other derivatives. The Company and the Guarantors shall cause any Notes so repurchased (other than Notes repurchased pursuant to cash-settled swaps or other derivatives) to be surrendered to the Trustee for cancellation in accordance with Section 2.08.

ARTICLE 3
Satisfaction and Discharge

Section 3.01 *Satisfaction and Discharge.* This Indenture and the Notes shall upon request of the Company contained in an Officer's Certificate cease to be of further effect, and the Trustee, at the expense of the Company, shall execute such instruments reasonably requested by the Company acknowledging satisfaction and discharge of this Indenture and the Notes, when (a) (i) all Notes theretofore authenticated and delivered (other than (x) Notes which have been destroyed, lost or stolen and which have been replaced, paid or exchanged for cash, Ordinary Shares or a combination thereof as provided in Section 2.06 and (y) Notes for whose payment money has theretofore been deposited in trust or segregated and held in trust by the Company and thereafter repaid to the Company or discharged from such trust, as provided in Section 4.04(d)) have been delivered to the Trustee for cancellation; or (ii) the Company or the Guarantors have deposited with the Trustee or delivered to Holders, as applicable, after the Notes have become due and payable, whether on the Maturity Date, any Redemption Date, any Fundamental Change Repurchase Date, upon exchange or otherwise, cash, Ordinary Shares or a combination thereof, as applicable, solely to satisfy the Company's Exchange Obligation, sufficient to pay all of the outstanding Notes and all other sums due and payable under this Indenture by the Company or the Guarantors; and (b) the Company has delivered to the Trustee

an Officer's Certificate and an Opinion of Counsel, each stating that all conditions precedent herein provided for relating to the satisfaction and discharge of this Indenture have been complied with. Notwithstanding the satisfaction and discharge of this Indenture, the obligations of the Company and the Guarantors to the Trustee under Section 7.06 shall survive.

ARTICLE 4
Particular Covenants of the Company

Section 4.01 *Payment of Principal and Interest.* The Company covenants and agrees that it will cause to be paid the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, and any accrued and unpaid interest on, each of the Notes at the places, at the respective times and in the manner provided herein and in the Notes.

Section 4.02 *Maintenance of Office or Agency.* The Company will maintain in the United States of America an office or agency where the Notes may be surrendered for registration of transfer or exchange or for presentation for payment or repurchase ("**Paying Agent**") or for exchange for cash, Ordinary Shares or a combination thereof ("**Exchange Agent**") and where notices and demands to or upon the Company or the Guarantors in respect of the Notes, the Guarantee and this Indenture may be made. The Company will give prompt written notice to the Trustee of the location, and any change in the location, of such office or agency. If at any time the Company shall fail to maintain any such required office or agency or shall fail to furnish the Trustee with the address thereof, such presentations, surrenders, notices and demands may be made at the Corporate Trust Office or any other office or agency in the United States of America so designated by the Trustee as a place where Notes may be presented for payment or for registration of transfer.

The Company may also from time to time designate as Paying Agent, Exchange Agent, or co-Note Registrars one or more other offices or agencies where the Notes may be presented or surrendered for any or all such purposes and may from time to time rescind such designations; *provided* that no such designation or rescission shall in any manner relieve the Company of its obligation to maintain an office or agency in the United States of America so designated by the Trustee as a place for such purposes. The Company will give prompt written notice to the Trustee of any such designation or rescission and of any change in the location of any such other office or agency. The terms "**Paying Agent**" and "**Exchange Agent**" include any such additional or other offices or agencies, as applicable.

The Company hereby initially designates the Trustee as the Paying Agent, Note Registrar, Custodian and Exchange Agent and the Corporate Trust Office as the office or agency in the United States of America where Notes may be surrendered for registration of transfer or exchange or for presentation for payment or repurchase or for exchange for cash, Ordinary Shares or a combination thereof and where notices and demands to or upon the Company or the Guarantors in respect of the Notes, the Guarantee and this Indenture may be made.

In acting hereunder and in connection with the Notes, the Paying Agent, the Custodian, the Exchange Agent, and the Note Registrar shall act solely as agent of the Company and will not assume any fiduciary duty or obligation towards or relationship of agency or trust for or with any of the owners or Holders of the Notes.

Section 4.03 *Appointments to Fill Vacancies in Trustee's Office.* The Company, whenever necessary to avoid or fill a vacancy in the office of Trustee, will appoint, in the manner provided in Section 7.09, a trustee, so that there shall at all times be a Trustee hereunder.

Section 4.04 *Provisions as to Paying Agent.* (a) If the Company shall appoint a Paying Agent other than the Trustee, the Company will cause such Paying Agent to execute and deliver to the Trustee an instrument in which such agent shall agree with the Trustee, subject to the provisions of this Section 4.04:

(i) that it will hold all sums held by it as such agent for the payment of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, and any accrued and unpaid interest on, the Notes in trust for the benefit of the Holders of the Notes;

(ii) that it will give the Trustee prompt written notice of any failure by the Company to make any payment of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, and any accrued and unpaid interest on, the Notes when the same shall be due and payable; and

(iii) that at any time during the continuance of an Event of Default, upon request of the Trustee, it will forthwith pay to the Trustee all sums so held in trust.

The Company shall, on or before each due date of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, or any accrued and unpaid interest on, the Notes, deposit with the Paying Agent a sum sufficient to pay such principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) or any such accrued and unpaid interest, and (unless such Paying Agent is the Trustee) the Company will promptly notify the Trustee in writing of any failure to take such action; *provided* that if such deposit is made on the due date, such deposit must be received by the Paying Agent by 11:00 a.m., New York City time, on such date; *provided, further*, that to the extent such deposit is received by the Paying Agent after 11:00 a.m. New York City time, on any such due date, such deposit will be deemed deposited on the next Business Day.

(b) If the Company shall act as its own Paying Agent, it will, on or before each due date of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, and any accrued and unpaid interest on, the Notes, set aside, segregate and hold in trust for the benefit of the Holders of the Notes a sum sufficient to pay such principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable)

and any such accrued and unpaid interest so becoming due and will promptly notify the Trustee in writing of any failure to take such action and of any failure by the Company to make any payment of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, or any accrued and unpaid interest on, the Notes when the same shall become due and payable.

(c) Anything in this Section 4.04 to the contrary notwithstanding, the Company may, at any time, for the purpose of obtaining a satisfaction and discharge of this Indenture, or for any other reason, pay, cause to be paid or deliver to the Trustee all sums or amounts held in trust by the Company or any Paying Agent hereunder as required by this Section 4.04, such sums or amounts to be held by the Trustee upon the trusts herein contained and upon such payment or delivery by the Company or any Paying Agent to the Trustee, the Company or such Paying Agent shall be released from all further liability but only with respect to such sums or amounts.

(d) Subject to applicable abandoned property laws, any money and Ordinary Shares deposited with the Trustee or any Paying Agent, or then held by the Company, in trust for the payment of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, any accrued and unpaid interest on and the consideration due upon exchange of any Note and remaining unclaimed for two years after such principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable), any such interest or such consideration due upon exchange has become due and payable shall be paid or delivered, as the case may be, to the Company on request of the Company contained in an Officer's Certificate, or (if then held by the Company) shall be discharged from such trust; and the Holder of such Note shall thereafter, as an unsecured general creditor, look only to the Company for payment thereof, and all liability of the Trustee or such Paying Agent with respect to such trust money and Ordinary Shares, and all liability of the Company as trustee thereof, shall thereupon cease.

(e) Upon the occurrence of any Event of Default specified in Section 6.01(i) or Section 6.01(j), the Trustee shall automatically be the Paying Agent.

Section 4.05 *Existence.* Subject to Article 11, each of the Company and Iterum shall do or cause to be done all things necessary to preserve and keep in full force and effect its corporate existence.

Section 4.06 *Rule 144A and Rule 144 Information Requirement.* At any time Iterum is not subject to Section 13 or 15(d) of the Exchange Act, Iterum shall, so long as any of the Notes or any Ordinary Shares delivered upon exchange thereof shall, at such time, constitute "restricted securities" within the meaning of Rule 144(a)(3) under the Securities Act, promptly provide to the Trustee and, upon written request, provide to any Holder, beneficial owner or prospective purchaser of such Notes or any Ordinary Shares delivered upon exchange of such Notes, the information required to be delivered pursuant to Rule 144A(d)(4) under the Securities Act to

facilitate the resale of such Notes or Ordinary Shares pursuant to Rule 144A and the information required to be delivered pursuant to Rule 144(c) under the Securities Act to facilitate the resale of such Notes pursuant to Rule 144.

Section 4.07 *Stay, Extension and Usury Laws.* Each of the Company and the Guarantors covenant (to the extent that it may lawfully do so) that it shall not at any time insist upon, plead, or in any manner whatsoever claim or take the benefit or advantage of, any stay, extension or usury law or other law that would prohibit or forgive the Company from paying all or any portion of the principal of or any interest on the Notes as contemplated herein, wherever enacted, now or at any time hereafter in force, or that may affect the covenants or the performance of this Indenture; and the Company and the Guarantors (to the extent they may lawfully do so) hereby expressly waive all benefit or advantage of any such law, and covenants that it will not, by resort to any such law, hinder, delay or impede the execution of any power herein granted to the Trustee, but will suffer and permit the execution of every such power as though no such law had been enacted.

Section 4.08 *Compliance Certificate; Statements as to Defaults.* The Company shall deliver to the Trustee within 120 days after the end of each fiscal year of the Company (beginning with the fiscal year ended on December 31, 2020) an Officer's Certificate stating (i) that a review has been conducted of the activity by the Company and the Guarantors and their respective performances under this Indenture, the Guarantee and the Notes and (ii) whether the signers thereof have knowledge of any Default that has occurred during the previous year and, if so, specifying each such Default and the nature thereof.

In addition, the Company shall deliver to the Trustee, as soon as possible, and in any event within 30 days after the Company becomes aware of the occurrence of any Event of Default or Default, an Officer's Certificate setting forth the details of such Event of Default or Default, its status and the action that the Company or the Guarantors are taking or proposing to take in respect thereof.

Section 4.09 *Further Instruments and Acts.* Upon request of the Trustee, the Exchange Agent or the Paying Agent, the Company will execute and deliver such further instruments and do such further acts as may be reasonably necessary or proper to carry out more effectively the purposes of this Indenture.

Section 4.10 *Tax Matters; Organizational Limitations*. In order to comply with applicable tax laws, rules and regulations (inclusive of directives, guidelines and interpretations promulgated by competent authorities) in effect from time to time ("**Applicable Tax Law**") the Company agrees (a) to provide to the Trustee sufficient information within its control about Holders or other applicable parties and/or transactions (including any modification to the terms of such transactions) so the Trustee can determine whether it has tax related obligations under Applicable Tax Law, (b) that the Trustee shall be entitled to make any withholding or deduction

from payments under this Indenture to the extent necessary to comply with Applicable Tax Law for which the Trustee shall not have any liability, and (c) to hold harmless the Trustee for any losses it may suffer due to the actions it takes to comply with such Applicable Tax Law. The Company agrees to provide in writing to each Holder, within 75 days following the end of each calendar year, the amount of original issue discount attributable to such Holder. The terms of this Section shall survive the termination of this Indenture. At all times at which any Note is outstanding, Iterum shall (a) maintain, directly or indirectly, 100% equity ownership of the Company and the Subsidiary Guarantors, and (b) cause the Company to elect to be treated as a disregarded entity for U.S. federal income tax purposes (and, in each case, neither Iterum nor the Company shall take any action that is inconsistent with the foregoing); provided that if the Company is held indirectly by Iterum, the Company shall be considered as disregarded as a separate entity from Iterum for U.S. federal income tax purposes.

Section 4.11 *Negative Covenants*. As long as any Notes remain outstanding, neither Iterum, the Guarantors or any of their Subsidiaries shall take any of the actions set forth in clauses (a) through (j) of this Section 4.11 (the "**Restricted Actions**"), unless Iterum shall have (i) provided at least 10 days' prior written notice thereof to the Holders (including the Major Investors), and (ii) obtained the prior written consent (evidenced as provided in Article 8) of the Holders of at least the Specified Percentage of the aggregate principal amount of the Notes then outstanding (determined in accordance with Article 8 and including consents obtained in connection with a repurchase of, or tender or exchange offer for, Notes); provided, that notwithstanding receipt of such consent of the Specified Percentage, if prior to the expiration of such 10 day period the Major Investors cause a Veto Notice to be delivered to Iterum, neither Iterum, the Guarantors or any of their Subsidiaries shall take the applicable Restricted Action. For purposes of this Indenture, a "**Veto Notice**" means a written notice delivered to Iterum stating that one or more Restricted Actions has been vetoed, with such notice being executed by holders of at least 30% of the outstanding Notes which must include the Major Investors so long as the Major Investors (collectively and together with their Affiliates) own at least 10% of the outstanding Notes.

(a) the creation, incurrence, issuance or assumption, directly or indirectly, of any new Indebtedness after the date of this Indenture, except for Permitted Indebtedness;

(b) solely with respect to Iterum, directly or through any Affiliate, the redemption, repurchase or other acquisition of any of Capital Stock except (i) redemptions, repurchases or other acquisitions of the Capital Stock of current or former employees, directors or consultants (or their estates or beneficiaries under their estates) pursuant to stock repurchase agreements, stock purchase plans, restricted stock agreements, stock rights plans, director or consultant stock option plans, or similar plans, or otherwise upon such Person's death, disability, retirement or termination of employment (for cash, by the cancellation of indebtedness or otherwise), (ii) any Capital Stock that, by its terms (or by the terms of any security into which it is convertible, or for which it is exchangeable, in each case, at the option of the holder of the Capital Stock), or upon

the happening of any event, matures or is mandatorily redeemable, pursuant to a sinking fund obligation or otherwise, or redeemable at the option of the holder of the Capital Stock, in whole or in part, (iii) conversions of any convertible securities into other securities pursuant to the terms of such convertible securities or otherwise in exchange thereof or conversion of preferred shares into ordinary shares (the securities referred to in clauses (ii) and (iii), "**Convertible/Redeemable Securities**"), and (iv) cash payments in lieu of the issuance of fractional shares upon conversion of convertible securities;

(c) the issuance or authorization to issue of any Convertible/Redeemable Securities which are not outstanding as of the date of this Indenture other than the Notes and the RLNs;

(d) (i) the entering into of one or more new joint ventures, collaborations, exclusive selling arrangements, strategic alliances or other similar partnerships or (ii) the sale, transfer or assignment of any assets that are material to the business of the Guarantors and their Subsidiaries, taken as a whole, other than (A) sales, transfers or assignments of assets as among the Company and any Guarantor or among Guarantors, (B) sales of inventory in the ordinary course of the business of the Guarantors and their Subsidiaries, (C) pursuant to dispositions of obsolete, surplus or worn out assets that are no longer useful in conduct of their business or (D) transactions wholly outside the United States involving development, marketing, distribution, services, sponsored research, collaboration, technology licensing or co-promotion agreements, strategic alliances or other non-U.S. corporate partnering transactions, including, sub-licensing or assignment of any non-U.S. rights under the Pfizer License;

(e) The occurrence of a Change of Control Transaction, other than a Change of Control Transaction in which each Holder of an outstanding Note receives cash consideration of at least 300% of the outstanding principal amount of such Note;

(f) The entering into of any amendment of, the waiver of any rights under, the agreement to the termination of any rights or provisions under, or the agreement to the assignment of any rights or delegation of duties under, the Pfizer Agreement, unless such amendment, waiver, termination, assignment or delegation (i) is in connection with a Change of Control Transaction, (ii) would not adversely affect the rights or interests of the Holders or (iii) is solely for purposes of a transaction described in clauses (A), (B), (C) or (D) of Section 4.11(d);

(g) The acquisition (whether by merger, consolidation, acquisition of stock or assets or otherwise), directly or indirectly, of any Person, business, division, securities or material assets, other than the acquisition of assets and materials in the ordinary course of business;

(h) The making of any loans, advances or capital contributions to, or investments in, any other Person, other than (i) advances of expenses to employees or contractors in the ordinary course of business, (ii) the formation of one or more new wholly-owned Subsidiary for the purposes of continuation of the existing business of the Guarantors and their Subsidiaries, or (iii)

loans, advances or capital contributions to and among the Guarantors, between the Company and the Guarantors or between the Company or the Guarantors and their wholly-owned Subsidiaries;

(i) The entering into of any transaction between any such entity, on the one hand, and any Significant Shareholder (for the avoidance of doubt, not including the Company, the Guarantors, or any of their Subsidiaries), on the other hand; provided, however, that the terms set forth in this clause (i) shall not apply to (I) the issuance of Notes in connection with the Rights Offering, (II) the issuance of Ordinary Shares upon exchange of any Notes or (III) any agreements or arrangements existing on the date of this Indenture or contemplated thereby; and

(j) any change or amendment to the terms of Subordinated Indebtedness unless such change or amendment (i) is permitted pursuant to the definition of "Permitted Indebtedness" or (ii) does not materially and adversely affect the rights or interests of the Holders.

Section 4.12 *Payment for Consent*. The Company and the Guarantors shall not, and shall not cause or permit any of their Subsidiaries to, directly or indirectly, pay or cause to be paid any consideration, whether by way of interest, fee or otherwise, to any Holder of any Notes for or as an inducement to any consent, waiver or amendment of any of the terms or provisions of this Indenture, the Notes, the Guarantees or the Investor Rights Agreement unless such consideration is offered to be paid (or agreed to be paid) and is paid to all Holders which so consent, waive or agree to amend in the time frame set forth in solicitation documents relating to such consent, waiver or agreement.

ARTICLE 5
Lists of Holders and Reports by the Company and the Trustee

Section 5.01 *Lists of Holders.* The Company covenants and agrees that it will, in accordance with Section 312 of the Trust Indenture Act, furnish or cause to be furnished to the Trustee or any Paying Agent, twice annually, not more than 15 days prior to June 30 and December 31 in each year beginning with June 30, 2020, and at such other times as the Trustee may request in writing, within 30 days after receipt by the Company of any such request (or such lesser time as the Trustee may reasonably request in order to enable it to timely provide any notice to be provided by it hereunder), a list in such form as the Trustee may reasonably require of the names and addresses of the Holders as of a date not more than 15 days (or such other date as the Trustee may reasonably request in order to so provide any such notices) prior to the time such information is furnished, except that no such list need be furnished so long as the Trustee is acting as Note Registrar.

Section 5.02 *Preservation and Disclosure of Lists; Communications to Holders.*

(a) The Trustee shall preserve, in as current a form as is reasonably practicable, all information as to the names and addresses of the Holders contained in the most recent list furnished to it as provided in Section 5.01 or maintained by the Trustee in its capacity as Note

Registrar, if so acting. The Trustee may destroy any list furnished to it as provided in Section 5.01 upon receipt of a new list so furnished.

(b) The rights of the Holders to communicate with other Holders with respect to their rights under this Indenture and the corresponding rights and privileges of the Trustee shall be as provided by Section 312(b)(2) of the Trust Indenture Act, if applicable.

(c) Every Holder of Notes, by receiving and holding the same, agrees with the Company and the Trustee that neither the Company nor the Trustee shall be deemed to be in violation of law or held accountable by reason of the disclosure of any such information as to the names and addresses of the Holders made pursuant to the Trust Indenture Act (if applicable) regardless of the source from which such information was derived.

Section 5.03 *Reports by Trustee*.

(a) Within 90 days after December 31 of each year commencing with the December 31 following the date of this Indenture, the Trustee shall transmit to all Holders such reports concerning the Trustee and its actions under this Indenture as may be required pursuant to the Trust Indenture Act to the extent and in the manner provided pursuant thereto and shall send a copy of any such report to the Holders. The Trustee shall also comply with Section 313(b)(2) of the Trust Indenture Act, if applicable. The Trustee shall also deliver all reports as required by Section 313(c) of the Trust Indenture Act, if applicable.

(b) A copy of each such report shall, at the time of such transmission to the Holders, be filed by the Trustee with each stock exchange, if any, upon which the Notes are listed, with the Commission and also with the Company. The Company will promptly notify the Trustee when the Notes are listed on any stock exchange.

Section 5.04 *Reports by the Company.*

(a) Each of the Guarantors and the Company covenants to comply with Section 314(a) of the Trust Indenture Act insofar as it relates to information, documentation and other reports which the Guarantors or the Company may be required to file with the Commission pursuant to Section 13 or Section 15(d) of the Exchange Act.

(b) The Company shall file with the Trustee, within 15 days after the same are filed with the Commission, copies of any documents or reports that Iterum is required to file with the Commission pursuant to Section 13 or 15(d) of the Exchange Act (excluding any such information, documents or reports, or portions thereof, subject to confidential treatment and any correspondence with the Commission). Any such document or report that Iterum files with the Commission via the Commission's EDGAR system shall be deemed to be filed with the Trustee for purposes of this Section 5.04(b) at the time such documents are filed via the EDGAR system,

it being understood that the Trustee shall not be responsible for determining whether such filings have been made.

(c) Delivery of the reports and documents described in subsection (b) above to the Trustee is for informational purposes only, and the Trustee's receipt of such shall not constitute constructive notice of any information contained therein or determinable from information contained therein, including the Company's or any Guarantor's compliance with any of its covenants hereunder (as to which the Trustee is entitled to conclusively rely on an Officer's Certificate).

ARTICLE 6
Defaults and Remedies

Section 6.01 *Events of Default.* Each of the following events shall be an "**Event of Default**" with respect to the Notes:

(a) default in any payment of principal or interest on any Note when due and payable on the Maturity Date, upon Optional Redemption, upon any required repurchase, upon declaration of acceleration or otherwise, where the default continues for a period of five Business Days;

(b) failure by the Company to comply with its obligation to exchange the Notes in accordance with this Indenture, and such failure continues for three Business Days subject to Section 14.01(c);

(c) failure by the Company to issue a Fundamental Change Company Notice in accordance with Section 15.02(c) or a Mandatory Exchange Notice in accordance with Section 14.01(b) when due;

(d) failure by the Company or any Guarantor to comply with their respective obligations under Article 11, Section 4.11 or Section 4.12;

(e) failure by the Company or any Guarantor for 60 days after written notice from the Trustee or the Holders of at least 25% in aggregate principal amount of the Notes then outstanding has been received by the Company to comply with any of their respective other agreements contained in the Notes, this Indenture or the Guarantee;

(f) default by any Guarantor or any Subsidiary of any Guarantor with respect to any mortgage, agreement or other instrument under which there may be outstanding, or by which there may be secured or evidenced, any indebtedness for money borrowed in excess of $5,000,000 (or its foreign currency equivalent) in the aggregate of the Guarantors and/or any such Subsidiary, whether such indebtedness now exists or shall hereafter be created (i) resulting in such indebtedness becoming or being declared due and payable or (ii) constituting a failure to

pay the principal or interest of any such debt when due and payable at its stated maturity, upon required repurchase, upon declaration of acceleration or otherwise, if such default is not cured or waived, or such acceleration is not rescinded, as the case may be, within 30 days after written notice to the Company from the Trustee or the Holders of at least 25% in aggregate principal amount of the Notes then outstanding in accordance with this Indenture;

(g) default by the Company or the Guarantors with respect to the RLNs, if such default is not cured or waived within 30 days after written notice to the Company from the Trustee or the Holders of at least 25% in principal amount of Notes then outstanding in accordance with this Indenture or the Guarantee;

(h) a final judgment or judgments for the payment of $5,000,000 (or its foreign currency equivalent) or more (excluding any amounts covered by insurance) in the aggregate rendered against any Guarantor or any Subsidiary of the Guarantors, which judgment is not discharged, satisfied, paid, waived or stayed within 60 days after (i) the date on which the right to appeal thereof has expired if no such appeal has commenced, or (ii) the date on which all rights to appeal have been extinguished;

(i) any Guarantor, the Company or any Significant Subsidiary shall commence a voluntary case or other proceeding seeking liquidation, reorganization or other relief with respect to any such Guarantor, the Company or any such Significant Subsidiary or its debts under any bankruptcy, insolvency or other similar law now or hereafter in effect or seeking the appointment of a trustee, receiver, liquidator, custodian or other similar official of any such Guarantor, the Company or any such Significant Subsidiary or any substantial part of its property, or shall consent to any such relief or to the appointment of or taking possession by any such official in an involuntary case or other proceeding commenced against it, or shall make a general assignment for the benefit of creditors, or shall fail generally to pay its debts as they become due;

(j) an involuntary case or other proceeding shall be commenced against any Guarantor, the Company or any Significant Subsidiary seeking liquidation, reorganization or other relief with respect to such Guarantor, the Company or such Significant Subsidiary or its debts under any bankruptcy, insolvency or other similar law now or hereafter in effect or seeking the appointment of a trustee, receiver, liquidator, custodian or other similar official of such Guarantor, the Company or such Significant Subsidiary or any substantial part of its property, and such involuntary case or other proceeding shall remain undismissed and unstayed for a period of 30 consecutive days; or

(k) the Guarantee shall be held in any judicial proceeding to be unenforceable or invalid or shall cease for any reason to be in full force and effect or any Guarantor, or any Person acting on behalf of any Guarantor, shall deny or disaffirm its obligations under the Indenture or the Guarantee.

Section 6.02 *Acceleration; Rescission and Annulment.* If one or more Events of Default shall have occurred and be continuing (whatever the reason for such Event of Default and whether it shall be voluntary or involuntary or be effected by operation of law or pursuant to any judgment, decree or order of any court or any order, rule or regulation of any administrative or governmental body), then, and in each and every such case (other than an Event of Default specified in Section 6.01(i) or Section 6.01(j) with respect to the Guarantors, the Company or a Significant Subsidiary), unless the principal of all of the Notes shall have already become due and payable, either the Trustee or the Holders of at least 25% in aggregate principal amount of the Notes then outstanding determined in accordance with Section 8.04, by notice in writing to the Company (and to the Trustee if given by Holders), may (and the Trustee, at the written request of such Holders, shall) declare 100% of the principal of, and any accrued and unpaid interest on, all the Notes to be due and payable immediately, and upon any such declaration the same shall become and shall automatically be immediately due and payable, anything contained in this Indenture or in the Notes to the contrary notwithstanding. If an Event of Default specified in Section 6.01(i) or Section 6.01(j) with respect to the Guarantors, the Company or a Significant Subsidiary occurs and is continuing, 100% of the principal of, and accrued and unpaid interest, if any, on, all Notes shall become and shall automatically be immediately due and payable.

The immediately preceding paragraph, however, is subject to the conditions that if, at any time after the principal of the Notes shall have been so declared due and payable, and before any judgment or decree for the payment of the monies due shall have been obtained or entered as hereinafter provided, the Company shall pay or shall deposit with the Trustee a sum sufficient to pay installments of any accrued and unpaid interest upon all Notes and the principal of any and all Notes that shall have become due otherwise than by acceleration (with interest on overdue installments of accrued and unpaid interest, and on such principal at the rate borne by the Notes at such time to the extent such interest is permitted by law) and amounts due to the Trustee pursuant to Section 7.06, and if (1) rescission would not conflict with any judgment or decree of a court of competent jurisdiction and (2) any and all existing Events of Default under this Indenture, other than the nonpayment of the principal of and accrued and unpaid interest, if any, on Notes that shall have become due solely by such acceleration, shall have been cured or waived pursuant to Section 6.09, then and in every such case (except as provided in the immediately succeeding sentence) the Holders of the Specified Percentage in aggregate principal amount of the Notes then outstanding, by written notice to the Company and to the Trustee, may waive all Defaults or Events of Default with respect to the Notes and rescind and annul such declaration and its consequences and such Default shall cease to exist, and any Event of Default arising therefrom shall be deemed to have been cured for every purpose of this Indenture; but no such waiver or rescission and annulment shall extend to or shall affect any subsequent Default or Event of Default, or shall impair any right consequent thereon. Notwithstanding anything to the contrary herein, no such waiver or rescission and annulment shall extend to or shall affect any Default or Event of Default resulting from (i) the nonpayment of the principal of, or accrued and unpaid interest on, any Notes, (ii) a failure to repurchase any Notes when required or (iii) a

failure to pay or deliver or cause to be delivered, as the case may be, the consideration due upon exchange of the Notes.

Section 6.03 *Special Interest*. Notwithstanding anything in this Indenture or in the Notes to the contrary, to the extent the Company elects, the sole remedy for an Event of Default relating to the Company's failure to comply with its obligations as set forth in Section 5.04 shall, for the first 360 days after the occurrence of such an Event of Default (and, for the avoidance of doubt, giving effect to the 60-day period set forth in Section 6.01(e)), consist exclusively of the right to receive Special Interest on the Notes at a rate equal to (i) 0.25% per annum of the principal amount of the Notes outstanding for each day during the first 180 calendar days after the occurrence of such an Event of Default during which such Event of Default is continuing (or, if earlier, the date on which such Event of Default is cured or waived as provided for in this Indenture) and (ii) 0.50% per annum of the principal amount of the Notes outstanding for each day from, and including, the 181st calendar day to, but excluding, the 360th calendar day after the occurrence of such an Event of Default during which such Event of Default is continuing (or, if earlier, the date on which such Event of Default is cured or waived as provided for in this Indenture). If the Company elects to pay Special Interest, such Special Interest shall be payable as set forth in Section 2.03(b). On the 361st day after such Event of Default (if the Event of Default relating to the Company's failure to comply with its obligations as set forth in Section 5.04 is not cured or waived prior to such 361st day), the Notes shall be immediately subject to acceleration as provided in Section 6.02. In the event the Company does not elect to pay Special Interest following an Event of Default in accordance with this Section 6.03 or the Company elected to make such payment but does not pay the Special Interest when due, the Notes shall be immediately subject to acceleration as provided in Section 6.02.

In order to elect to pay Special Interest as the sole remedy during the first 360 days after the occurrence of any Event of Default described in the immediately preceding paragraph, the Company must notify in writing all Holders of the Notes, the Trustee and the Paying Agent of such election prior to the beginning of such 360-day period. Upon the failure to timely give such notice, the Notes shall be immediately subject to acceleration as provided in Section 6.02.

In no event shall Special Interest accrue under the terms of this Indenture at a rate per year in excess of 0.50%, regardless of the number of events or circumstances giving rise to the requirement to pay such Special Interest.

This Section 6.03 shall not affect the rights of Holders in the event of the occurrence of any other Event of Default.

Section 6.04 *Payments of Notes on Default; Suit Therefor.* If an Event of Default described in clause (a) of Section 6.01 shall have occurred, the Company shall, upon demand of the Trustee, pay to the Trustee, for the benefit of the Holders of the Notes, the whole amount then due and payable on the Notes for principal and interest, if any, with interest on any overdue

principal and interest, if any, at the rate borne by the Notes at such time (to the extent such interest on overdue principal and interest is permitted by law), and, in addition thereto, such further amount as shall be sufficient to cover any amounts due to the Trustee under Section 7.06. If the Company shall fail to pay such amounts forthwith upon such demand, the Trustee, in its own name and as trustee of an express trust, may institute a judicial proceeding for the collection of the sums so due and unpaid, may prosecute such proceeding to judgment or final decree and may enforce the same against the Company, any Guarantor or any other obligor upon the Notes and collect the moneys adjudged or decreed to be payable in the manner provided by law out of the property of the Company, the Guarantors or any other obligor upon the Notes, wherever situated.

In the event there shall be pending proceedings for the bankruptcy or for the reorganization of the Company, any Guarantor or any other obligor on the Notes under Title 11 of the United States Code, or any other applicable law, or in case a receiver, assignee or trustee in bankruptcy or reorganization, liquidator, sequestrator or similar official shall have been appointed for or taken possession of the Company, any Guarantor or such other obligor, the property of the Company, such Guarantor or such other obligor, or in the event of any other judicial proceedings relative to the Company, such Guarantor or such other obligor upon the Notes, or to the creditors or property of the Company, such Guarantor or such other obligor, the Trustee, irrespective of whether the principal of the Notes shall then be due and payable as therein expressed or by declaration or otherwise and irrespective of whether the Trustee shall have made any demand pursuant to the provisions of this Section 6.04, shall be entitled and empowered, by intervention in such proceedings or otherwise, to file and prove a claim or claims for the whole amount of principal and accrued and unpaid interest, if any, in respect of the Notes, and, in case of any judicial proceedings, to file such proofs of claim and other papers or documents and to take such other actions as it may deem necessary or advisable in order to have the claims of the Trustee (including any claim for the reasonable compensation, expenses, disbursements and advances of the Trustee, its agents and counsel) and of the Holders allowed in such judicial proceedings relative to the Company, any Guarantor or any other obligor on the Notes, its or their creditors, or its or their property, and to collect and receive any monies or other property payable or deliverable on any such claims, and to distribute the same after the deduction of any amounts due to the Trustee under Section 7.06; and any receiver, assignee or trustee in bankruptcy or reorganization, liquidator, custodian or similar official is hereby authorized by each of the Holders to make such payments to the Trustee, as administrative expenses, and, in the event that the Trustee shall consent to the making of such payments directly to the Holders, to pay to the Trustee any amount due it for reasonable compensation, expenses, advances and disbursements, including agents and counsel fees, and including any other amounts due to the Trustee under Section 7.06, incurred by it up to the date of such distribution. To the extent that such payment of reasonable compensation, expenses, advances and disbursements out of the estate in any such proceedings shall be denied for any reason, payment of the same shall be secured by a lien on, and shall be paid out of, any and all distributions, dividends, monies, securities and other property that the Holders of the Notes may be entitled to receive in such

proceedings, whether in liquidation or under any plan of reorganization or arrangement or otherwise.

Nothing herein contained shall be deemed to authorize the Trustee to authorize or consent to or accept or adopt on behalf of any Holder any plan of reorganization, arrangement, adjustment or composition affecting such Holder or the rights of any Holder thereof, or to authorize the Trustee to vote in respect of the claim of any Holder in any such proceeding.

All rights of action and of asserting claims under this Indenture, or under any of the Notes, may be enforced by the Trustee without the possession of any of the Notes, or the production thereof at any trial or other proceeding relative thereto, and any such suit or proceeding instituted by the Trustee shall be brought in its own name as trustee of an express trust, and any recovery of judgment shall, after provision for the payment of the reasonable compensation, expenses, disbursements and advances of the Trustee, its agents and counsel, be for the ratable benefit of the Holders of the Notes.

In any proceedings brought by the Trustee (and in any proceedings involving the interpretation of any provision of this Indenture to which the Trustee shall be a party) the Trustee shall be held to represent all the Holders of the Notes, and it shall not be necessary to make any Holders of the Notes parties to any such proceedings.

In case the Trustee shall have proceeded to enforce any right under this Indenture and such proceedings shall have been discontinued or abandoned because of any waiver pursuant to Section 6.09 or any rescission and annulment pursuant to Section 6.02 or for any other reason or shall have been determined adversely to the Trustee, then and in every such case the Company, the Guarantors, the Holders and the Trustee shall, subject to any determination in such proceeding, be restored respectively to their several positions and rights hereunder, and all rights, remedies and powers of the Company, the Guarantors, the Holders and the Trustee shall continue as though no such proceeding had been instituted.

Section 6.05 *Application of Monies Collected by Trustee.* Any monies or property collected by the Trustee pursuant to this Article 6 with respect to the Notes shall be applied in the following order, at the date or dates fixed by the Trustee for the distribution of such monies or property, upon presentation of the several Notes, and stamping thereon the payment, if only partially paid, and upon surrender thereof, if fully paid:

First, to the payment of all amounts due the Trustee, the Exchange Agent and the Paying Agent under this Indenture;

Second, to holders of Senior Debt to the extent required by Article 18;

Third, in case the principal of the outstanding Notes shall not have become due and be unpaid, to the payment of any interest on, and any cash due upon exchange of, the Notes in

default in the order of the date due of the payments of such interest and cash due upon exchange, as the case may be, with interest (to the extent that such interest is permitted by applicable law and has been collected by the Trustee) upon such overdue amounts at the rate borne by the Notes at such time, such payments to be made ratably to the Persons entitled thereto;

Fourth, in case the principal of the outstanding Notes shall have become due, by declaration or otherwise, and be unpaid, to the payment of the whole amount (including, if applicable, the payment of the Redemption Price and the Fundamental Change Repurchase Price and any cash due upon exchange) then owing and unpaid upon the Notes for principal and interest, if any, with interest on the overdue principal and (to the extent that such interest is permitted by applicable law and has been collected by the Trustee) upon such overdue installments of interest at the rate borne by the Notes at such time, and in case such monies shall be insufficient to pay in full the whole amounts so due and unpaid upon the Notes, then to the payment of such principal (including, if applicable, the Redemption Price and the Fundamental Change Repurchase Price and the cash due upon exchange) and any interest without preference or priority of principal over any interest, or of any interest over principal, or of any installment of interest over any other installment of interest, or of any Note over any other Note, ratably to the aggregate of such principal (including, if applicable, the Redemption Price and the Fundamental Change Repurchase Price and any cash due upon exchange) and any accrued and unpaid interest; and

Fifth, to the payment of the remainder, if any, to the Company.

Section 6.06 *Proceedings by Holders.* Except to enforce the right to receive payment of principal (including, if applicable, the Redemption Price and the Fundamental Change Repurchase Price) or interest when due, or the right to receive payment or delivery of the consideration due upon exchange, no Holder of any Note shall have any right by virtue of or by availing of any provision of this Indenture to institute any suit, action or proceeding in equity or at law upon or under or with respect to this Indenture, or for the appointment of a receiver, trustee, liquidator, custodian or other similar official, or for any other remedy hereunder, unless:

(a) such Holder previously shall have given to the Trustee written notice of an Event of Default and of the continuance thereof, as herein provided;

(b) Holders of at least 25% in aggregate principal amount of the Notes then outstanding shall have made written request upon the Trustee to institute such action, suit or proceeding in its own name as Trustee hereunder;

(c) such Holders shall have offered to the Trustee such security and/or indemnity satisfactory to it against any loss, liability or expense to be incurred therein or thereby;

(d) the Trustee has not complied with such request for 60 days after its receipt of such notice, request and offer of security and/or indemnity; and

(e) no direction that, in the opinion of the Trustee, is inconsistent with such written request shall have been given to the Trustee by the Holders of the Specified Percentage of the aggregate principal amount of the Notes then outstanding within such 60-day period pursuant to Section 6.09,

it being understood and intended, and being expressly covenanted by the taker and Holder of every Note with every other taker and Holder and the Trustee that no one or more Holders shall have any right in any manner whatever by virtue of or by availing of any provision of this Indenture to affect, disturb or prejudice the rights of any other Holder, or to obtain or seek to obtain priority over or preference to any other such Holder, or to enforce any right under this Indenture, except in the manner herein provided and for the equal, ratable and common benefit of all Holders (except as otherwise provided herein), it being understood that the Trustee does not have an affirmative duty to ascertain whether or not any actions or forbearances by a Holder are prejudicial to other Holders. For the protection and enforcement of this Section 6.06, each and every Holder and the Trustee shall be entitled to such relief as can be given either at law or in equity.

Notwithstanding any other provision of this Indenture and any provision of any Note, the right of any Holder to receive payment or delivery, as the case may be, of (x) the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, (y) accrued and unpaid interest, if any, on, and (z) the consideration due upon exchange of, such Note, on or after the respective due dates expressed or provided for in such Note or in this Indenture, or to institute suit for the enforcement of any such payment or delivery, as the case may be, on or after such respective dates against each of the Company and any Guarantor shall not be impaired or affected without the consent of such Holder.

Section 6.07 *Proceedings by Trustee.* In case of an Event of Default, the Trustee may in its discretion proceed to protect and enforce the rights vested in it by this Indenture by such appropriate judicial proceedings as are necessary to protect and enforce any of such rights, either by suit in equity or by action at law or by proceeding in bankruptcy or otherwise, whether for the specific enforcement of any covenant or agreement contained in this Indenture or in aid of the exercise of any power granted in this Indenture, or to enforce any other legal or equitable right vested in the Trustee by this Indenture or by law.

Section 6.08 *Remedies Cumulative and Continuing.* Except as provided in the last paragraph of Section 2.06, all powers and remedies given by this Article 6 to the Trustee or to the Holders shall, to the extent permitted by law, be deemed cumulative and not exclusive of any thereof or of any other powers and remedies available to the Trustee or the Holders of the Notes, by judicial proceedings or otherwise, to enforce the performance or observance of the covenants and agreements contained in this Indenture, and no delay or omission of the Trustee or of any Holder of any of the Notes to exercise any right or power accruing upon any Default or Event of Default shall impair any such right or power, or shall be construed to be a waiver of any such

Default or Event of Default or any acquiescence therein; and, subject to the provisions of Section 6.06, every power and remedy given by this Article 6 or by law to the Trustee or to the Holders may be exercised from time to time, and as often as shall be deemed expedient, by the Trustee or by the Holders.

Section 6.09 *Direction of Proceedings and Waiver of Defaults by Holders.* The Holders of the Specified Percentage of the aggregate principal amount of the Notes at the time outstanding determined in accordance with Section 8.04 shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the Trustee or exercising any trust or power conferred on the Trustee with respect to the Notes; *provided*, *however*, that (a) such direction shall not be in conflict with any rule of law or with this Indenture, and (b) the Trustee may take any other action deemed proper by the Trustee that is not inconsistent with such direction. The Trustee may refuse to follow any direction that it determines is unduly prejudicial to the rights of any other Holder (it being understood that the Trustee does not have an affirmative duty to ascertain whether or not any actions or forbearances by a Holder are prejudicial to other Holders) or that would involve the Trustee in personal liability. Prior to taking any action hereunder, the Trustee shall be entitled to indemnification and/or security from the Holders satisfactory to it against all losses, liabilities, or expenses caused by taking or not taking such action. The Holders of the Specified Percentage in aggregate principal amount of the Notes at the time outstanding (determined in accordance with Section 8.04 and including waivers obtained in connection with a repurchase of, or tender or exchange offer for, the Notes) may on behalf of the Holders of all of the Notes waive any past Default or Event of Default hereunder and its consequences except (i) a default in the payment of accrued and unpaid interest, if any, on, or the principal (including any Redemption Price and any Fundamental Change Repurchase Price) of, the Notes when due that has not been cured, (ii) a failure by the Company to pay, deliver or cause to deliver, as the case may be, the consideration due upon exchange of the Notes or (iii) a default in respect of a covenant or provision hereof which under Article 10 cannot be modified or amended without the consent of each Holder of an outstanding Note affected. Upon any such waiver the Company, the Guarantors, the Trustee and the Holders of the Notes shall be restored to their former positions and rights hereunder; but no such waiver shall extend to any subsequent or other Default or Event of Default or impair any right consequent thereon. Whenever any Default or Event of Default hereunder shall have been waived as permitted by this Section 6.09, said Default or Event of Default shall for all purposes of the Notes and this Indenture be deemed to have been cured and to be not continuing.

Section 6.10 *Notice of Defaults.*

(a) Upon the Company becoming aware of the occurrence of any Event of Default or the occurrence of any event, circumstance or condition that following notice or the lapse of time provided for under Section 6.01 would constitute an Event of Default, the Company shall as soon as possible, and in any event within 15 Business Days after becoming aware of any such

occurrence, file with the Trustee written notice of such Event of Default or event, circumstance or condition.

(b) The Trustee shall, within 90 days after any Event of Default for which it receives written notice as provided for in Section 6.10(a), send to all Holders as the names and addresses of such Holders appear upon the Note Register (as provided under Section 313(c) of the Trust Indenture Act, if applicable), notice of such Event of Default or other event, circumstance or condition, unless such Event of Default or other event, circumstance or condition shall have been cured or waived before the giving of such notice.

Section 6.11 *Undertaking to Pay Costs.* All parties to this Indenture agree, and each Holder of any Note by its acceptance thereof shall be deemed to have agreed, that any court may, in its discretion, require, in any suit for the enforcement of any right or remedy under this Indenture, or in any suit against the Trustee for any action taken or omitted by it as Trustee, the filing by any party litigant in such suit of an undertaking to pay the costs of such suit and that such court may in its discretion assess reasonable costs, including reasonable attorneys' fees and expenses, against any party litigant in such suit, having due regard to the merits and good faith of the claims or defenses made by such party litigant; *provided* that the provisions of this Section 6.11 (to the extent permitted by law) shall not apply to any suit instituted by the Trustee, to any suit instituted by any Holder, or group of Holders, holding in the aggregate more than 10% in principal amount of the Notes at the time outstanding determined in accordance with Section 8.04, or to any suit instituted by any Holder for the enforcement of the payment of the principal of or accrued and unpaid interest, if any, on any Note (including, but not limited to, the Redemption Price and the Fundamental Change Repurchase Price with respect to the Notes being repurchased as provided in this Indenture) on or after the due date expressed or provided for in such Note or to any suit for the enforcement of the right to exchange any Note in accordance with the provisions of Article 14.

ARTICLE 7
Concerning the Trustee

Section 7.01 *Duties and Responsibilities of Trustee.* The Trustee, prior to the occurrence of an Event of Default and after the curing or waiver of all Events of Default that may have occurred, undertakes to perform such duties and only such duties as are specifically set forth in this Indenture. In the event an Event of Default has occurred and is continuing, the Trustee shall exercise such of the rights and powers vested in it by this Indenture, and use the same degree of care and skill in its exercise, as a prudent person would exercise or use under the circumstances in the conduct of such person's own affairs; *provided* that if an Event of Default occurs and is continuing, the Trustee will be under no obligation to exercise any of the rights or powers under this Indenture at the request or direction of any of the Holders unless such Holders have offered to the Trustee indemnity and/or security satisfactory to it against any loss, liability or expense that might be incurred by it in compliance with such request or direction.

No provision of this Indenture shall be construed to relieve the Trustee from liability for its own negligent action, its own negligent failure to act or its own willful misconduct, except that:

(a) prior to the occurrence of an Event of Default and after the curing or waiving of all Events of Default that may have occurred:

(i) the duties and obligations of the Trustee shall be determined solely by the express provisions of this Indenture, and the Trustee shall not be liable except for the performance of such duties and obligations as are specifically set forth in this Indenture and no implied covenants or obligations shall be read into this Indenture against the Trustee; and

(ii) in the absence of bad faith or willful misconduct on the part of the Trustee, the Trustee may conclusively rely, as to the truth of the statements and the correctness of the opinions expressed therein, upon any certificates or opinions furnished to the Trustee and conforming to the requirements of this Indenture; but, in the case of any such certificates or opinions that by any provisions hereof are specifically required to be furnished to the Trustee, the Trustee shall be under a duty to examine the same to determine whether or not they conform to the requirements of this Indenture (but need not confirm or investigate the accuracy of any mathematical calculations or other facts stated therein);

(b) the Trustee shall not be liable for any error of judgment made in good faith by a Responsible Officer or Officers of the Trustee, unless it shall be proved that the Trustee was negligent in ascertaining the pertinent facts;

(c) the Trustee shall not be liable with respect to any action taken or omitted to be taken by it in good faith in accordance with the written direction of the Holders of not less than the Specified Percentage of the aggregate principal amount of the Notes at the time outstanding determined as provided in Section 8.04 relating to the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred upon the Trustee, under this Indenture;

(d) whether or not therein provided, every provision of this Indenture relating to the conduct or affecting the liability of, or affording protection to, the Trustee shall be subject to the provisions of this Section 7.01;

(e) the Trustee shall not be liable in respect of any payment (as to the correctness of amount, entitlement to receive or any other matters relating to payment) or notice effected by the Company, any Guarantor or any Paying Agent or any records maintained by any co-Note Registrar with respect to the Notes;

(f) if any party fails to deliver a notice relating to an event the fact of which, pursuant to this Indenture, requires notice to be sent to the Trustee, the Trustee may conclusively rely on its failure to receive such notice as reason to act as if no such event occurred, unless a Responsible Officer of the Trustee had actual knowledge of such event;

(g) in the absence of written investment direction from the Company, all cash received by the Trustee shall be placed in a non-interest bearing trust account, and in no event shall the Trustee be liable for the selection of investments or for investment losses fees, taxes or other charges incurred thereon or for losses incurred as a result of the liquidation of any such investment prior to its maturity date or the failure of the party directing such investments prior to its maturity date or the failure of the party directing such investment to provide timely written investment direction, and the Trustee shall have no obligation to invest or reinvest any amounts held hereunder in the absence of such written investment direction from the Company;

(h) the rights, privileges, immunities, benefits and protections afforded to the Trustee pursuant to this Article 7 shall also be afforded to the Trustee in each of its capacities hereunder, and each agent, custodian, and other Person employed to act hereunder, including, without limitation, in its capacities as Custodian, Note Registrar, Paying Agent, Exchange Agent or transfer agent hereunder; and

(i) in the event that the Trustee is also acting as Custodian, Note Registrar, Paying Agent, Exchange Agent, or transfer agent hereunder, the rights and protections afforded to the Trustee pursuant to this Article 7 shall also be afforded to such Custodian, Note Registrar, Paying Agent, Exchange Agent or transfer agent.

None of the provisions contained in this Indenture shall require the Trustee to expend or risk its own funds or otherwise incur personal financial liability in the performance of any of its duties or in the exercise of any of its rights or powers.

Section 7.02 *Reliance on Documents, Opinions, Etc.* In furtherance of and subject to the Trust Indenture Act and except as otherwise provided in Section 7.01:

(a) the Trustee may conclusively rely and shall be fully protected in acting upon any resolution, certificate, statement, instrument, opinion, report, notice, request, consent, order, bond, note, coupon or other paper or document believed by it in good faith to be genuine and to have been signed or presented by the proper party or parties;

(b) any request, direction, order or demand of the Company or any Guarantor mentioned herein shall be sufficiently evidenced by an Officer's Certificate of the Company or such Guarantor (unless other evidence in respect thereof be herein specifically prescribed); and any Board Resolution of the Company or such Guarantor may be evidenced to the Trustee by a copy thereof certified by the Secretary or an Assistant Secretary of the Company or such Guarantor, as applicable;

(c) the Trustee may consult with counsel of its selection and require an Opinion of Counsel and any advice of such counsel or Opinion of Counsel shall be full and complete authorization and protection in respect of any action taken or omitted by it hereunder in good faith and in reliance on such advice or Opinion of Counsel;

(d) the Trustee shall not be bound to make any investigation into the facts or matters stated in any resolution, certificate, statement, instrument, opinion, report, notice, request, direction, consent, order, bond, debenture or other paper or document, but the Trustee, in its discretion, may make such further inquiry or investigation into such facts or matters as it may see fit, and, if the Trustee shall determine to make such further inquiry or investigation, it shall be entitled to examine the books, records and premises of the Company or the Guarantors, personally or by agent or attorney at the expense of the Company or the Guarantors and shall incur no liability of any kind by reason of such inquiry or investigation;

(e) the Trustee may execute any of the trusts or powers hereunder or perform any duties hereunder either directly or by or through agents, custodians, nominees or attorneys and the Trustee shall not be responsible for any misconduct or negligence on the part of any agent, custodian, nominee or attorney appointed by it with due care hereunder;

(f) the permissive rights of the Trustee enumerated herein shall not be construed as duties;

(g) the Trustee shall not be required to give any bond or surety in respect of the performance of its powers and duties hereunder;

(h) the Trustee may request that the Company or any Guarantor deliver a certificate setting forth the names of individuals and/or titles of officers authorized at such time to take specified actions pursuant to this Indenture; which certificate may be signed by any Person authorized to sign an Officer's Certificate for the Company or the Guarantors, as applicable, including any Person specified as so authorized in any such certificate previously delivered and not superseded;

(i) the Trustee will not be responsible or liable for any action it takes or omits to take in good faith that it believes to be authorized or within the rights or powers conferred upon it by this Indenture;

(j) before the Trustee acts or refrains from acting, it may require an Officer's Certificate or an Opinion of Counsel or both. Except as otherwise provided herein, the Trustee shall not be responsible or liable for any action it takes, suffers or omits to take in good faith in reliance on such Officer's Certificate or Opinion of Counsel; and

(k) the Trustee will be under no obligation to exercise any of the rights or powers vested in it by this Indenture at the request or direction of any of the Holders unless such Holders

have offered to the Trustee indemnity and/or security satisfactory to the Trustee against the losses, liabilities and expenses that might be incurred by it in compliance with such request or direction.

In no event shall the Trustee be liable or responsible for any special, indirect, consequential or punitive loss or damage of any kind whatsoever (including but not limited to lost profits), even if the Trustee has been advised of the likelihood of such loss or damage and regardless of the form of action.

The Trustee shall not be charged with knowledge of any Default or Event of Default with respect to the Notes, unless either (1) a Responsible Officer shall have actual knowledge of such Default or Event of Default or (2) written notice of such Default or Event of Default shall have been received by a Responsible Officer of the Trustee at the Corporate Trust Office and such notice references the Notes, the Company, Iterum, and this Indenture.

Section 7.03 *No Responsibility for Recitals, Etc.* The recitals contained herein and in the Notes (except in the Trustee's certificate of authentication) shall be taken as the statements of the Company and the Guarantors, and the Trustee assumes no responsibility for the correctness of the same. The Trustee makes no representations as to the validity or sufficiency of this Indenture, of the Guarantee or of the Notes. The Trustee shall not be accountable for the use or application by the Company of any Notes or the proceeds of any Notes authenticated and delivered by the Trustee in conformity with the provisions of this Indenture.

Section 7.04 *Trustee, Paying Agents, Exchange Agents or Note Registrar May Own Notes.* The Trustee, any Paying Agent, any Exchange Agent, Note Registrar, in its individual or any other capacity, may become the owner or pledgee of Notes with the same rights it would have if it were not the Trustee, Paying Agent, Exchange Agent or Note Registrar.

Section 7.05 *Monies and Ordinary Shares to Be Held in Trust.* All monies and any Ordinary Shares received by the Trustee shall, until used or applied as herein provided, be held in trust for the purposes for which they were received. Money and Ordinary Shares held by the Trustee in trust hereunder need not be segregated from other funds or property except to the extent required by law. The Trustee shall be under no liability for any interest on any money or Ordinary Shares received by it hereunder except as may be agreed from time to time by the Company and the Trustee.

Section 7.06 *Compensation and Expenses of Trustee.* The Company, Iterum, Iterum U.S. Limited and Iterum U.S. Holding, jointly and severally, covenant and agree to pay to the Trustee, in any capacity under this Indenture, from time to time, and the Trustee shall be entitled to, compensation for all services rendered by it hereunder in any capacity (which shall not be limited by any provision of law in regard to the compensation of a trustee of an express trust) as mutually agreed to in writing between the Trustee and the Company, and the Company will pay or reimburse the Trustee upon its request for all reasonable expenses, disbursements and

advances reasonably incurred or made by the Trustee in accordance with any of the provisions of this Indenture in any capacity thereunder (including the reasonable compensation and the expenses and disbursements of its agents and counsel and of all Persons not regularly in its employ) except any such expense, disbursement or advance as shall have been caused by its negligence or willful misconduct (as determined by a final, non-appealable decision of a court of competent jurisdiction). The Company, Iterum, Iterum U.S. Limited and Iterum U.S. Holding, jointly and severally, covenant to indemnify the Trustee (which for purposes of this Section 7.06 shall include its officers, directors, employees, successors, assigns, agents, successors and assigns) in any capacity under this Indenture and any other document or transaction entered into in connection herewith and its agents and any authenticating agent for, and to hold them harmless against, any loss, claim (whether asserted by the Company, any Guarantor, a Holder or any Person), damage, liability or expense (including reasonable and documented out-of-pocket attorneys' fees) incurred without negligence or willful misconduct (as determined by a final, non-appealable decision of a court of competent jurisdiction) on the part of the Trustee, its officers, directors, agents or employees, or such agent or authenticating agent, as the case may be, as determined by a final, non-appealable decision of a court of competent jurisdiction, and arising out of or in connection with the acceptance or administration of this Indenture or in any other capacity hereunder, including the costs and expenses of defending themselves against any claim of liability (including, without limitation, any and all reasonable and documented out-of-pocket attorneys' fees and expenses) or enforcing the Company's obligations hereunder (whether such claims arise by or are against the Company, the Guarantors, or a third person). The obligations of the Company, Iterum, Iterum U.S. Limited and Iterum U.S. Holding under this Section 7.06 to compensate or indemnify the Trustee and to pay or reimburse the Trustee for expenses, disbursements and advances shall be secured by a senior claim to which the Notes are hereby made subordinate on all money or property held or collected by the Trustee, except, subject to the effect of Section 6.05, funds held in trust herewith for the benefit of the Holders of particular Notes. The Trustee's right to receive payment of any amounts due under this Section 7.06 shall not be subordinate to any other liability or indebtedness of Iterum, and to secure the payment obligations under this Section 7.06 the Trustee shall have a lien prior to the Notes on all money or property held or collected by the Trustee, in its capacity as the Trustee, other than money or property held in trust to pay principal of and interest, if any, on particular Notes. The obligations of the Company, Iterum, Iterum U.S. Limited and Iterum U.S. Holding under this Section 7.06 shall survive the satisfaction and discharge of this Indenture and the earlier resignation or removal or the Trustee. Neither the Company nor any Guarantor shall be required to pay for any settlement made without its consent, which consent shall not be unreasonably withheld. The indemnification provided in this Section 7.06 shall extend to the officers, directors, agents and employees of the Trustee and any successor Trustee hereunder.

Without prejudice to any other rights available to the Trustee under applicable law, when the Trustee and its agents and any authenticating agent incur expenses or render services after an Event of Default specified in Section 6.01(i) or Section 6.01(j) occurs, the expenses and the

compensation for the services are intended to constitute expenses of administration under any bankruptcy, insolvency or similar laws.

Section 7.07 *Officer's Certificate as Evidence.* Except as otherwise provided in Section 7.01, whenever in the administration of the provisions of this Indenture the Trustee shall deem it necessary or desirable that a matter be proved or established prior to taking or omitting any action hereunder, such matter (unless other evidence in respect thereof be herein specifically prescribed) may, in the absence of negligence and willful misconduct on the part of the Trustee, be deemed to be conclusively proved and established by an Officer's Certificate delivered to the Trustee, and such Officer's Certificate, in the absence of negligence and willful misconduct on the part of the Trustee, shall be full warrant to the Trustee for any action taken or omitted by it under the provisions of this Indenture upon the faith thereof.

Section 7.08 *Eligibility of Trustee.* There shall at all times be a Trustee hereunder which shall be a Person that is eligible pursuant to the Trust Indenture Act to act as such and has a combined capital and surplus of at least $50,000,000. If such Person publishes reports of condition at least annually, pursuant to law or to the requirements of any supervising or examining authority, then for the purposes of this Section 7.08, the combined capital and surplus of such Person shall be deemed to be its combined capital and surplus as set forth in its most recent report of condition so published. If at any time the Trustee shall cease to be eligible in accordance with the provisions of this Section 7.08, it shall resign immediately in the manner and with the effect hereinafter specified in this Article 7.

Section 7.09 *Resignation or Removal of Trustee.* (a) The Trustee may at any time resign by giving written notice of such resignation to the Company and by delivering notice thereof to the Holders at their addresses as they shall appear on the Note Register. Upon receiving such notice of resignation, the Company shall promptly appoint a successor trustee by written instrument, in duplicate, executed by order of the Company's Board of Directors, one copy of which instrument shall be delivered to the resigning Trustee and one copy to the successor trustee. If no successor trustee shall have been so appointed and have accepted appointment within 60 days after the sending of such notice of resignation to the Holders, the resigning Trustee may, upon 10 Business Days' notice to the Company and the Holders and at the expense of the Company, petition any court of competent jurisdiction for the appointment of a successor trustee, or any Holder who has been a bona fide holder of a Note or Notes for at least six months may, subject to the provisions of Section 6.11, on behalf of himself or herself and all others similarly situated, petition any such court for the appointment of a successor trustee. Such court may thereupon, after such notice, if any, as it may deem proper and prescribe, appoint a successor trustee.

(b) In case at any time any of the following shall occur:

(i) the Trustee shall cease to be eligible in accordance with the provisions of Section 7.08 and shall fail to resign after written request therefor by the Company or by any such Holder, or

(ii) the Trustee shall become incapable of acting, or shall be adjudged a bankrupt or insolvent, or a receiver of the Trustee or of its property shall be appointed, or any public officer shall take charge or control of the Trustee or of its property or affairs for the purpose of rehabilitation, conservation or liquidation,

then, in either case, the Company may by a Board Resolution remove the Trustee and appoint a successor trustee by written instrument, in duplicate, executed by order of the Company's Board of Directors, one copy of which instrument shall be delivered to the Trustee so removed and one copy to the successor trustee, or, subject to the provisions of Section 6.11, any Holder who has been a bona fide holder of a Note or Notes for at least six months may, on behalf of himself or herself and all others similarly situated, petition any court of competent jurisdiction for the removal of the Trustee and the appointment of a successor trustee. Such court may thereupon, after such notice, if any, as it may deem proper and prescribe, remove the Trustee and appoint a successor trustee.

(c) The Holders of the Specified Percentage in aggregate principal amount of the Notes at the time outstanding, as determined in accordance with Section 8.04, may at any time remove the Trustee and nominate a successor trustee that shall be deemed appointed as successor trustee unless within 10 days after notice to the Company of such nomination the Company objects thereto, in which case the Trustee so removed or any Holder, upon the terms and conditions and otherwise as in Section 7.09(a) provided and at the expense of Iterum, may petition any court of competent jurisdiction for an appointment of a successor trustee.

(d) Any resignation or removal of the Trustee and appointment of a successor trustee pursuant to any of the provisions of this Section 7.09 shall become effective upon acceptance of appointment by the successor trustee as provided in Section 7.10.

Section 7.10 *Acceptance by Successor Trustee.* Any successor trustee appointed as provided in Section 7.09 shall execute, acknowledge and deliver to the Company and to its predecessor trustee an instrument accepting such appointment hereunder, and thereupon the resignation or removal of the predecessor trustee shall become effective and such successor trustee, without any further act, deed or conveyance, shall become vested with all the rights, powers, duties and obligations of its predecessor hereunder, with like effect as if originally named as Trustee herein; but, nevertheless, on the written request of the Company or of the successor trustee, the trustee ceasing to act shall, upon payment of any amounts then due it pursuant to the provisions of Section 7.06, execute and deliver an instrument transferring to such successor trustee all the rights and powers of the trustee so ceasing to act. Upon request of any such successor trustee, the Company and the Guarantors shall execute any and all instruments in

writing for more fully and certainly vesting in and confirming to such successor trustee all such rights and powers. Any trustee ceasing to act shall, nevertheless, retain a senior claim to which the Notes are hereby made subordinate on all money or property held or collected by such trustee as such, except for funds held in trust for the benefit of Holders of particular Notes, to secure any amounts then due it pursuant to the provisions of Section 7.06.

No successor trustee shall accept appointment as provided in this Section 7.10 unless at the time of such acceptance such successor trustee shall be eligible under the provisions of Section 7.08.

Upon acceptance of appointment by a successor trustee as provided in this Section 7.10, each of the Company and the successor trustee, at the written direction and at the expense of the Company shall send or cause to be sent notice of the succession of such trustee hereunder to the Holders at their addresses as they shall appear on the Note Register. If the Company fails to send such notice within 10 days after acceptance of appointment by the successor trustee, the successor trustee shall cause such notice to be sent at the expense of the Company.

Section 7.11 *Succession by Merger, Etc.* Any corporation or other entity into which the Trustee may be merged or converted or with which it may be consolidated, or any corporation or other entity resulting from any merger, conversion or consolidation to which the Trustee shall be a party, or any corporation or other entity succeeding to all or substantially all of the corporate trust business of the Trustee (including the administration of this Indenture), shall be the successor to the Trustee hereunder without the execution or filing of any paper or any further act on the part of any of the parties hereto; *provided* that in the case of any corporation or other entity succeeding to all or substantially all of the corporate trust business of the Trustee such corporation or other entity shall be eligible under the provisions of Section 7.08.

In case at the time such successor to the Trustee shall succeed to the trusts created by this Indenture, any of the Notes shall have been authenticated but not delivered, any such successor to the Trustee may adopt the certificate of authentication of any predecessor trustee or authenticating agent appointed by such predecessor trustee, and deliver such Notes so authenticated; and in case at that time any of the Notes shall not have been authenticated, any successor to the Trustee or an authenticating agent appointed by such successor trustee may authenticate such Notes either in the name of any predecessor trustee hereunder or in the name of the successor trustee; and in all such cases such certificates shall have the full force which it is anywhere in the Notes or in this Indenture provided that the certificate of the Trustee shall have; *provided*, *however*, that the right to adopt the certificate of authentication of any predecessor trustee or to authenticate Notes in the name of any predecessor trustee shall apply only to its successor or successors by merger, conversion or consolidation.

Section 7.12 *Trustee's Application for Instructions from the Company.* Any application by the Trustee for written instructions from the Company (other than with regard to any action

proposed to be taken or omitted to be taken by the Trustee that affects the rights of the Holders of the Notes under this Indenture) may, at the option of the Trustee, set forth in writing any action proposed to be taken or omitted by the Trustee under this Indenture and the date on and/or after which such action shall be taken or such omission shall be effective. The Trustee shall not be liable for any action taken by, or omission of, the Trustee in accordance with a proposal included in such application on or after the date specified in such application (which date shall not be less than three Business Days after the date any officer that the Company has indicated to the Trustee should receive such application actually receives such application, unless any such officer shall have consented in writing to any earlier date), unless, prior to taking any such action (or the effective date in the case of any omission), the Trustee shall have received written instructions in accordance with this Indenture in response to such application specifying the action to be taken or omitted.

Section 7.13 *Disqualification; Conflicting Interests*.

(a) If applicable, to the extent that the Trustee or the Company determines that the Trustee has a conflicting interest within the meaning of the Trust Indenture Act, the Trustee shall immediately notify the Company of such conflict and, within 90 days after ascertaining that it has such conflicting interest, either eliminate such conflicting interest or resign to the extent and in the manner provided by, and subject to the provisions of, the Trust Indenture Act and this Indenture. The Company shall take prompt steps to have a successor appointed in the manner provided in this Indenture.

(b) If the Trustee fails to comply with Section 7.13(a), the Trustee shall, within 10 days of the expiration of such 90-day period, transmit a notice of such failure to the Holders in the manner and to the extent provided in the Trust Indenture Act and this Indenture.

(c) If the Trustee fails to comply with Section 7.13(a) after written request therefore by the Company or any Holder, then any Holder of any Note who has been a bona fide Holder for at least six (6) months may on behalf of himself or herself and all others similarly situated, petition any court of competent jurisdiction for the removal of such Trustee and the appointment of a successor Trustee.

Section 7.14 *Preferential Collection of Claims Against Company.* If and when the Trustee shall be or shall become a creditor, directly or indirectly, secured or unsecured, of the Company or the Guarantors (or any other obligor upon the Notes), excluding any creditor relationship set forth in Section 311(b) of the Trust Indenture Act, if applicable, the Trustee shall be subject to the applicable provisions of the Trust Indenture Act regarding the collection of claims against the Company or the Guarantors (or any such other obligor).

ARTICLE 8
Concerning the Holders

Section 8.01 *Action by Holders.* Whenever in this Indenture it is provided that the Holders of a specified percentage of the aggregate principal amount of the Notes may take any action (including the making of any demand or request, the giving of any notice, consent or waiver or the taking of any other action), the fact that at the time of taking any such action, the Holders of such specified percentage have joined therein may be evidenced (a) by any instrument or any number of instruments of similar tenor executed by Holders in person or by agent or proxy appointed in writing, or (b) by the record of the Holders voting in favor thereof at any meeting of Holders duly called and held in accordance with the provisions of Article 9, or (c) by a combination of such instrument or instruments and any such record of such a meeting of Holders. Whenever the Company or the Trustee solicits the taking of any action by the Holders of the Notes, the Company or the Trustee may, but shall not be required to, fix in advance of such solicitation, a date as the record date for determining Holders entitled to take such action. The record date if one is selected shall be not more than 15 days prior to the date of commencement of solicitation of such action.

Section 8.02 *Proof of Execution by Holders.* Subject to the provisions of Section 7.01, Section 7.02 and Section 9.05, proof of the execution of any instrument by a Holder or its agent or proxy shall be sufficient if made in accordance with such reasonable rules and regulations as may be prescribed by the Trustee or in such manner as shall be satisfactory to the Trustee. The holding of Notes shall be proved by the Note Register or by a certificate of the Note Registrar. The record of any Holders' meeting shall be proved in the manner provided in Section 9.06.

Section 8.03 *Who Are Deemed Absolute Owners.* The Company, the Trustee, any authenticating agent, any Paying Agent, any Exchange Agent and any Note Registrar may deem the Person in whose name a Note shall be registered upon the Note Register to be, and may treat it as, the absolute owner of such Note (whether or not such Note shall be overdue and notwithstanding any notation of ownership or other writing thereon made by any Person other than the Company or any Note Registrar) for the purpose of receiving payment of or on account of the principal of and (subject to Section 2.03) any accrued and unpaid interest on such Note, for exchange of such Note and for all other purposes under this Indenture; and neither the Company nor the Trustee nor any Paying Agent nor any Exchange Agent nor any Note Registrar shall be affected by any notice to the contrary. The sole registered holder of a Global Note shall be the Depositary or its nominee. All such payments or deliveries so made to any Holder for the time being, or upon its order, shall be valid, and, to the extent of the sums or Ordinary Shares so paid or delivered, effectual to satisfy and discharge the liability for monies payable or shares deliverable upon any such Note. Notwithstanding anything to the contrary in this Indenture or the Notes, following an Event of Default, any owner of a beneficial interest in a Global Note may directly enforce against the Company, without the consent, solicitation, proxy, authorization or any other action of the Depositary or any other Person, such Holder's right to exchange such

beneficial interest for a Note in certificated form in accordance with the provisions of this Indenture.

Section 8.04 *Certain Notes Disregarded.* In determining whether the Holders of the requisite aggregate principal amount of Notes have concurred in any direction, consent, waiver or other action under this Indenture, Notes that are owned by the Company, by the Guarantors, by any respective Subsidiary thereof or by any respective Affiliate thereof (provided that no Initial Purchaser shall be considered such an Affiliate for this purpose) shall be disregarded and deemed not to be outstanding for the purpose of any such determination; *provided* that for the purposes of determining whether the Trustee shall be protected in relying on any such direction, consent, waiver or other action only Notes that a Responsible Officer actually knows are so owned shall be so disregarded. Notes so owned that have been pledged in good faith may be regarded as outstanding for the purposes of this Section 8.04 if the pledgee shall establish to the satisfaction of the Trustee the pledgee's right to so act with respect to such Notes and that the pledgee is not the Company, any Guarantor, any respective Subsidiary thereof or any respective Affiliate thereof (provided that no Initial Purchaser shall be considered such an Affiliate for this purpose). In the case of a dispute as to such right, any decision or indecision by the Trustee taken upon the advice of counsel shall be full protection to the Trustee. Upon request of the Trustee, the Company shall furnish to the Trustee promptly an Officer's Certificate listing and identifying all Notes, if any, known by the Company to be owned or held by or for the account of any of the above described Persons; and, subject to Section 7.01, the Trustee shall be entitled to accept such Officer's Certificate as conclusive evidence of the facts therein set forth and of the fact that all Notes not listed therein are outstanding for the purpose of any such determination.

Section 8.05 *Revocation of Consents; Future Holders Bound.* At any time prior to (but not after) the evidencing to the Trustee, as provided in Section 8.01, of the taking of any action by the Holders of the percentage of the aggregate principal amount of the Notes specified in this Indenture in connection with such action, any Holder of a Note that is shown by the evidence to be included in the Notes the Holders of which have consented to such action may, by filing written notice with the Trustee at its Corporate Trust Office and upon proof of holding as provided in Section 8.02, revoke such action so far as concerns such Note. Except as aforesaid, any such action taken by the Holder of any Note shall be conclusive and binding upon such Holder and upon all future Holders and owners of such Note and of any Notes issued in exchange or substitution therefor or upon registration of transfer thereof, irrespective of whether any notation in regard thereto is made upon such Note or any Note issued in exchange or substitution therefor or upon registration of transfer thereof.

ARTICLE 9
Holders' Meetings

Section 9.01 *Purpose of Meetings.* A meeting of Holders may be called at any time and from time to time pursuant to the provisions of this Article 9 for any of the following purposes:

(a) to give any notice to the Company or to the Trustee or to give any directions to the Trustee permitted under this Indenture, or to consent to the waiving of any Default or Event of Default hereunder (in each case, as permitted under this Indenture) and its consequences, or to take any other action authorized to be taken by Holders pursuant to any of the provisions of Article 6;

(b) to remove the Trustee and nominate a successor trustee pursuant to the provisions of Article 7;

(c) to consent to the execution of an indenture or indentures supplemental hereto pursuant to the provisions of Section 10.02; or

(d) to take any other action authorized to be taken by or on behalf of the Holders of any specified aggregate principal amount of the Notes under any other provision of this Indenture or under applicable law.

Section 9.02 *Call of Meetings by Trustee.* The Trustee may at any time call a meeting of Holders to take any action specified in Section 9.01, to be held at such time and at such place as the Trustee shall determine. Notice of every meeting of the Holders, setting forth the time and the place of such meeting and in general terms the action proposed to be taken at such meeting and the establishment of any record date pursuant to Section 8.01, shall be sent to Holders of such Notes at their addresses as they shall appear on the Note Register. Such notice shall also be sent to the Company. Such notices shall be sent not less than 20 nor more than 90 days prior to the date fixed for the meeting.

Any meeting of Holders shall be valid without notice if the Holders of all Notes then outstanding are present in person or by proxy or if notice is waived before or after the meeting by the Holders of all Notes then outstanding, and if the Company and the Trustee are either present by duly authorized representatives or have, before or after the meeting, waived notice.

Section 9.03 *Call of Meetings by Company or Holders.* In case at any time the Company, pursuant to a Board Resolution, or the Holders of at least 10% of the aggregate principal amount of the Notes then outstanding, shall have requested the Trustee to call a meeting of Holders, by written request setting forth in reasonable detail the action proposed to be taken at the meeting, and the Trustee shall not have sent the notice of such meeting within 20 days after receipt of such request, then the Company or such Holders may determine the time and the place for such meeting and may call such meeting to take any action authorized in Section 9.01, by sending notice thereof as provided in Section 9.02.

Section 9.04 *Qualifications for Voting.* To be entitled to vote at any meeting of Holders a Person shall (a) be a Holder of one or more Notes on the record date pertaining to such meeting or (b) be a Person appointed by an instrument in writing as proxy by a Holder of one or more Notes on the record date pertaining to such meeting. The only Persons who shall be entitled to

be present or to speak at any meeting of Holders shall be the Persons entitled to vote at such meeting and their counsel and any representatives of the Trustee and its counsel and any representatives of the Company and its counsel.

Section 9.05 *Regulations.* Notwithstanding any other provisions of this Indenture, the Trustee may make such reasonable regulations as it may deem advisable for any meeting of Holders, in regard to proof of the holding of Notes and of the appointment of proxies, and in regard to the appointment and duties of inspectors of votes, the submission and examination of proxies, certificates and other evidence of the right to vote, and such other matters concerning the conduct of the meeting as it shall think fit.

The Trustee shall, by an instrument in writing, appoint a temporary chairman of the meeting, unless the meeting shall have been called by the Company or by Holders as provided in Section 9.03, in which case the Company or the Holders calling the meeting, as the case may be, shall in like manner appoint a temporary chairman. A permanent chairman and a permanent secretary of the meeting shall be elected by vote of the Holders of the Specified Percentage in aggregate principal amount of the Notes represented at the meeting and entitled to vote at the meeting.

Subject to the provisions of Section 8.04, at any meeting of Holders each Holder or proxyholder shall be entitled to one vote for each $1,000 principal amount of Notes held or represented by him or her; *provided*, *however*, that no vote shall be cast or counted at any meeting in respect of any Note challenged as not outstanding and ruled by the chairman of the meeting to be not outstanding. The chairman of the meeting shall have no right to vote other than by virtue of Notes held by it or instruments in writing as aforesaid duly designating it as the proxy to vote on behalf of other Holders. Any meeting of Holders duly called pursuant to the provisions of Section 9.02 or Section 9.03 may be adjourned from time to time by the Holders of the Specified Percentage of the aggregate principal amount of Notes represented at the meeting, whether or not constituting a quorum, and the meeting may be held as so adjourned without further notice.

Section 9.06 *Voting.* The vote upon any resolution submitted to any meeting of Holders shall be by written ballot on which shall be subscribed the signatures of the Holders or of their representatives by proxy and the outstanding aggregate principal amount of the Notes held or represented by them. The permanent chairman of the meeting shall appoint two inspectors of votes who shall count all votes cast at the meeting for or against any resolution and who shall make and file with the secretary of the meeting their verified written reports in duplicate of all votes cast at the meeting. A record in duplicate of the proceedings of each meeting of Holders shall be prepared by the secretary of the meeting and there shall be attached to said record the original reports of the inspectors of votes on any vote by ballot taken thereat and affidavits by one or more Persons having knowledge of the facts setting forth a copy of the notice of the meeting and showing that said notice was sent as provided in Section 9.02. The

record shall show the aggregate principal amount of the Notes voting in favor of or against any resolution. The record shall be signed and verified by the affidavits of the permanent chairman and secretary of the meeting and one of the duplicates shall be delivered to the Company and the other to the Trustee to be preserved by the Trustee, the latter to have attached thereto the ballots voted at the meeting.

Any record so signed and verified shall be conclusive evidence of the matters therein stated.

Section 9.07 *No Delay of Rights by Meeting.* Nothing contained in this Article 9 shall be deemed or construed to authorize or permit, by reason of any call of a meeting of Holders or any rights expressly or impliedly conferred hereunder to make such call, any hindrance or delay in the exercise of any right or rights conferred upon or reserved to the Trustee or to the Holders under any of the provisions of this Indenture or of the Notes. Nothing contained in this Article 9 shall be deemed or construed to limit any Holder's actions pursuant to the applicable procedures of the Depositary so long as the Notes are Global Notes.

ARTICLE 10
Supplemental Indentures

Section 10.01 *Supplemental Indentures Without Consent of Holders.* The Company and the Guarantors, when authorized by the resolutions of each of their respective Boards of Directors, and the Trustee, at the Company's expense, may from time to time and at any time enter into an indenture or indentures supplemental hereto for one or more of the following purposes:

(a) to cure any ambiguity, omission, defect or inconsistency;

(b) to provide for the assumption by a Successor Company of the obligations of the Company or the Guarantors under the Notes, this Indenture or the Guarantee pursuant to Article 11;

(c) to add additional guarantees and/or guarantors with respect to the Notes;

(d) to secure the Notes;

(e) to add to the covenants or Events of Default of the Company or the Guarantors for the benefit of the Holders or surrender any right or power conferred upon the Company or the Guarantors;

(f) to make any change that does not adversely affect the rights of any Holder;

(g) to adjust the Exchange Rate as provided in this Indenture;

(h) to provide for the acceptance of appointment by a successor trustee pursuant to Section 7.10 or to facilitate the administration of the trusts by more than one trustee;

(i) to irrevocably elect or eliminate a Settlement Method and/or irrevocably elect a minimum Specified Dollar Amount;

(j) to reflect the issuance of additional Notes as permitted by the Indenture;

(k) to make any changes or modifications necessary in connection with the registration of the Notes under the Securities Act; *provided*, *however*, that such action does not adversely affect the interests of the Holders of Notes in any material respect;

(l) to make any amendments or changes necessary to comply or maintain compliance with the Trust Indenture Act, if applicable; or

(m) in connection with any Specified Transaction, to provide that the Notes are exchangeable for Reference Property, subject to the provisions described in Section 14.02, and make certain related changes to the terms of the Notes to the extent expressly required under this Indenture.

Upon the written request of the Company and subject to Section 10.05, the Trustee is hereby authorized to, and shall join with the Company and the Guarantors in the execution of any such supplemental indenture, to make any further appropriate agreements and stipulations that may be therein contained, except that the Trustee shall not be obligated to, but may, enter into any supplemental indenture that affects the Trustee's own rights, duties, privileges, liabilities or immunities under this Indenture or otherwise.

Any supplemental indenture authorized by the provisions of this Section 10.01 may be executed by the Company, the Guarantors and the Trustee without the consent of the Holders of any of the Notes at the time outstanding, notwithstanding any of the provisions of Section 10.02.

Section 10.02 *Supplemental Indentures with Consent of Holders.* With the consent (evidenced as provided in Article 8) of the Holders of at least the Specified Percentage of the aggregate principal amount of the Notes then outstanding (determined in accordance with Article 8 and including consents obtained in connection with a repurchase of, or tender or exchange offer for, Notes), the Company and the Guarantors, when authorized by the resolutions of their respective Boards of Directors and the Trustee, at the Company's expense, may from time to time and at any time enter into an indenture or indentures supplemental hereto for the purpose of adding any provisions to or changing in any manner or eliminating any of the provisions of this Indenture or any supplemental indenture or of modifying in any manner the rights of the Holders; *provided*, *however*, that, without the consent of each Holder of an outstanding Note affected, no such supplemental indenture shall:

(a) reduce the amount or percentage of Notes whose Holders must consent to an amendment or to waive any past default, including any change to the definition of "Specified Percentage";

(b) reduce the rate of or extend the stated time for payment of interest on any Note;

(c) reduce the principal of or change the Maturity Date of any Note;

(d) make any change that adversely affects the exchange rights of any Notes;

(e) reduce the Redemption Price or the Fundamental Change Repurchase Price of any Note or amend or modify in any manner adverse to the Holders the Company's obligation to make such payments, whether through an amendment or waiver of provisions in the covenants, definitions or otherwise;

(f) make any Note payable in a currency or at a place of payment other than that stated in the Note;

(g) change any provision of this Indenture or the related definitions to affect the ranking of the Notes or any Guarantee;

(h) make any change in this Article 10 that requires each Holder's consent or in the waiver provisions in Section 6.02 or Section 6.09 or any other amendment or waiver processes in this Indenture;

(i) modify the Guarantee in any manner adverse to the Holders (including the release of any Guarantor from any of its obligations under its Guarantee or this Indenture); or

(j) make any change to Section 4.11 or Section 4.12.

Upon the written request of the Company, and upon the filing with the Trustee of evidence of the consent of Holders as aforesaid and subject to Section 10.05, the Trustee shall join with the Company and the Guarantors in the execution of such supplemental indenture unless such supplemental indenture affects the Trustee's own rights, duties or immunities under this Indenture or otherwise, in which case the Trustee may, but shall not be obligated to, enter into such supplemental indenture.

Holders do not need under this Section 10.02 to approve the particular form of any proposed supplemental indenture. It shall be sufficient if such Holders approve the substance thereof. After any such supplemental indenture becomes effective, the Company shall deliver to the Holders a notice briefly describing such supplemental indenture. However, the failure to give such notice to all the Holders, or any defect in the notice, will not impair or affect the validity of the supplemental indenture.

Section 10.03 *Effect of Supplemental Indentures.* Upon the execution of any supplemental indenture pursuant to the provisions of this Article 10, this Indenture shall be and be deemed to be modified and amended in accordance therewith and the respective rights, limitation of rights, obligations, privileges, duties and immunities under this Indenture of the Trustee, the Company, the Guarantors and the Holders shall thereafter be determined, exercised and enforced hereunder subject in all respects to such modifications and amendments and all the terms and conditions of any such supplemental indenture shall be and be deemed to be part of the terms and conditions of this Indenture for any and all purposes.

Section 10.04 *Notation on Notes.* Notes authenticated and delivered after the execution of any supplemental indenture pursuant to the provisions of this Article 10 may, at the Company's expense, bear a notation in form approved by the Trustee as to any matter provided for in such supplemental indenture. If the Company or the Trustee shall so determine, new Notes so modified as to conform, in the opinion of the Trustee and the Board of Directors of the Company, to any modification of this Indenture contained in any such supplemental indenture may, at the Company's expense, be prepared and executed by the Company, authenticated, upon receipt of a Company Order, by the Trustee (or an authenticating agent duly appointed by the Trustee pursuant to Section 17.10) and delivered in exchange for the Notes then outstanding, upon surrender of such Notes then outstanding.

Section 10.05 *Evidence of Compliance of Supplemental Indenture to Be Furnished to Trustee.* In addition to the documents required by Section 17.05, the Trustee shall receive an Officer's Certificate and an Opinion of Counsel as conclusive evidence that any supplemental indenture executed pursuant hereto complies with the requirements of this Article 10 and is permitted or authorized by this Indenture and that the supplemental indenture constitutes the legal, valid and binding obligation of the Company enforceable in accordance with its terms.

Section 10.06 *Conformity with Trust Indenture Act*. Every supplemental indenture executed pursuant to this Article shall conform to the applicable requirements of the Trust Indenture Act, if any.

ARTICLE 11
Consolidation, Merger, Sale, Conveyance and Lease

Section 11.01 *The Company and the Guarantors May Consolidate, Etc. on Certain Terms.* Subject to the provisions of Section 11.02, neither the Company nor any Guarantor shall consolidate with, merge with or into, or sell, convey, transfer or lease all or substantially all of their respective properties and assets to another Person, unless:

(a) the resulting, surviving or transferee Person (the "**Successor Company**"), if not the Company or a Guarantor, shall be a corporation organized and existing under the laws of the United States of America, any State thereof, the District of Columbia, the Republic of Ireland or Bermuda, and the Successor Company (if not the Company or a Guarantor) shall expressly

assume, by supplemental indenture all of the obligations of the Company or such Guarantor, as applicable, under the Notes, this Indenture and the Guarantee, as the case may be;

(b) immediately after giving effect to such transaction, no Default or Event of Default shall have occurred and be continuing under this Indenture; and

(c) in the case of a consolidation, merger, sale, conveyance, transfer or lease involving the Company or the Subsidiary Guarantors, the Successor Company is a wholly owned Subsidiary of Iterum.

For purposes of this Section 11.01, the sale, conveyance, transfer or lease of all or substantially all of the properties and assets of one or more Subsidiaries of Iterum to another Person, which properties and assets, if held by Iterum instead of such Subsidiaries, would constitute all or substantially all of the properties and assets of Iterum on a consolidated basis, shall be deemed to be the sale, conveyance, transfer or lease of all or substantially all of the properties and assets of Iterum to another Person. For the avoidance of doubt, any rights that may be available to the Holders pursuant to Section 15.02 shall not be waived or otherwise modified as a result of a Fundamental Change being permissible under this Section 11.01.

Section 11.02 *Successor Corporation to Be Substituted.* In case of any such consolidation, merger, sale, conveyance, transfer or lease and upon the assumption by the Successor Company, by supplemental indenture (if required by Section 11.01), executed and delivered to the Trustee and satisfactory in form to the Trustee, of the due and punctual payment of the principal of and any accrued and unpaid interest on all of the Notes, the due and punctual delivery or payment, as the case may be, of any consideration due upon exchange of the Notes and the due and punctual performance of all of the covenants and conditions of this Indenture, the Notes and the Guarantee to be performed by the Company or the Guarantors, as applicable, such Successor Company (if not the Company or any Guarantor, as applicable) shall succeed to and, except in the case of a lease of all or substantially all of the Company's or the Guarantors' properties and assets, shall be substituted for the Company or the Guarantor, as applicable, with the same effect as if it had been named herein as the party of the first part. Such Successor Company thereupon may cause to be signed, and may issue either in its own name or in the name of the Company any or all of the Notes issuable hereunder which theretofore shall not have been signed by the Company and delivered to the Trustee; and, upon the written order of such Successor Company instead of the Company and subject to all the terms, conditions and limitations in this Indenture prescribed, the Trustee shall authenticate and shall deliver, or cause to be authenticated and delivered, any Notes that previously shall have been signed and delivered by the Officers of the Company to the Trustee for authentication, and any Notes that such Successor Company thereafter shall cause to be signed and delivered to the Trustee for that purpose. All the Notes so issued shall in all respects have the same legal rank and benefit under this Indenture as the Notes theretofore or thereafter issued in accordance with the terms of this Indenture as though all of such Notes had been issued at the date of the execution hereof. In the

event of any such consolidation, merger, sale, conveyance or transfer (but not in the case of a lease), upon compliance with this Article 11 the Person named as the "Company", "Iterum" or a "Subsidiary Guarantor" in the first paragraph of this Indenture (or any successor that shall thereafter have become such in the manner prescribed in this Article 11), as applicable, may be dissolved, wound up and liquidated at any time thereafter and, except in the case of a lease, such Person shall be released from its liabilities as obligor or guarantor and (in the case of the Company) maker of the Notes and from its obligations under this Indenture, the Notes and the Guarantee, as the case may be.

In case of any such consolidation, merger, sale, conveyance, transfer or lease, such changes in phraseology and form (but not in substance) may be made in the Notes thereafter to be issued as may be appropriate.

Section 11.03 *Officer's Certificate and Opinion of Counsel to Be Given to Trustee.* No such consolidation, merger, sale, conveyance, transfer or lease shall be effective unless the Trustee shall receive an Officer's Certificate and an Opinion of Counsel as conclusive evidence that any such consolidation, merger, sale, conveyance, transfer or lease and any such assumption and, if a supplemental indenture is required in connection with such transaction, such supplemental indenture, complies with the provisions of this Article 11, and in the case of the Opinion of Counsel, that such supplemental indenture is the legal, valid and binding obligation of the relevant Successor Company.

Section 11.04 *Changes of Control*. Iterum shall require the ultimate beneficial owner or beneficial owners that controls or control, as the case may be, any acquiring Person or Persons, in any transaction permitted under this Indenture which constitutes a Change of Control Transaction with respect to Iterum, to guarantee the obligations of the Company and Iterum under this Indenture and the Guarantee as a condition to such transaction or series of related transactions; provided that the foregoing obligation may be waived by Holders of at least the Specified Percentage in principal amount of Notes then outstanding in accordance with this Indenture.

ARTICLE 12
Immunity of Incorporators, Shareholders, Officers and Directors

Section 12.01 *Indenture, Notes and Guarantee Solely Corporate Obligations.* No recourse for the payment of the principal of or any accrued and unpaid interest on any Note or in respect of the Guarantee, nor for any claim based thereon or otherwise in respect thereof, and no recourse under or upon any obligation, covenant or agreement of the Company or the Guarantors in this Indenture or in any supplemental indenture or in any Note or the Guarantee, nor because of the creation of any indebtedness represented thereby, shall be had against any incorporator, shareholder, employee, agent, Officer or director or Subsidiary (other than the Company or the Subsidiary Guarantors), as such, past, present or future, of the Company, the Guarantors or of

any of their respective successor corporations, either directly or through the Company, the Guarantors or any successor corporation, whether by virtue of any constitution, statute or rule of law, or by the enforcement of any assessment or penalty or otherwise; it being expressly understood that all such liability is hereby expressly waived and released as a condition of, and as a consideration for, the execution of this Indenture and the issuance of the Notes and the Guarantee.

ARTICLE 13
Guarantee of Notes

Section 13.01 *Guarantee.*

(a) By its execution hereof, each Guarantor acknowledges and agrees that it receives substantial benefits from the Company and the issuance of the Notes and that such Guarantor is providing its Guarantee for good and valuable consideration, including, without limitation, such substantial benefits. Accordingly, subject to the provisions of this Article 13, each Guarantor hereby fully and unconditionally guarantees as a primary principal obligation and not merely as a surety to each Holder and its successors and assigns that: (x) the principal of (including the Redemption Price and Fundamental Change Repurchase Price, if applicable), Exchange Obligations with respect to, and interest on, the Notes shall be duly and punctually paid in full and/or performed in accordance with the terms of this Indenture when due, whether at the Maturity Date, upon declaration of acceleration, upon redemption, upon required repurchase, upon exchange or otherwise, along with any interest on overdue principal, interest, and (to the extent permitted by law) interest on any interest, if any, on the Notes, (y) in case of any extension of time of payment or renewal of any Notes or any of such other obligations, the same shall be duly and punctually paid in full and/or performed in accordance with the terms of this Indenture when due or performed in accordance with the terms of the extension or renewal, whether at the Maturity Date, upon declaration of acceleration, upon redemption, upon required repurchase, upon exchange or otherwise, along with any interest on overdue principal, interest and (to the extent permitted by law) interest on any interest, if any, on the Notes. Furthermore, subject to the provisions of this Article 13, each Guarantor hereby fully and unconditionally guarantees to the Trustee and to each Holder and their respective successors and assigns that all other obligations of the Company to the Holders or the Trustee hereunder or under the Notes (including fees, expenses or other obligations) shall be promptly paid in full or performed, all in accordance with the terms hereof, subject, however, in the case of each of the foregoing obligations set forth above in this Section 13.01, to the limitations set forth in Section 13.02 hereof (the obligations set forth in this Section 13.01 collectively, the "**Guarantee Obligations**"). Failing payment when due of any Guarantee Obligation for whatever reason, such Guarantor will be obligated to pay the same immediately. An Event of Default with respect to the Notes under this Indenture shall constitute an event of default under the Guarantee and shall entitle the Holders to accelerate the obligations of the Guarantors hereunder in the same manner and to the same extent as the obligations of the Company. Each Guarantor covenants

and agrees, and each Holder of a Note, by such Holder's acceptance thereof, likewise covenants and agrees, that, notwithstanding anything in this Indenture or the Notes to the contrary, the Guarantee constitutes a general unsecured obligation of each Guarantor and will be subordinate in right of payment to any Guarantor Senior Debt, it being understood that the terms of Article 18 of this Indenture shall apply to the Guarantee Obligations as if (i) such Article 18 were set forth herein in full, (ii) the term "Guarantee Obligations" were substituted for the term "Notes" appearing in such Article 18, (iii) the term "Guarantor Senior Debt" were substituted for the term "Senior Debt" appearing in such Article 18 and (iv) the term "Guarantors" were substituted for the term "Company" appearing in such Article 18.

(b) Subject to the provisions of this Article 13, each Guarantor hereby agrees that its Guarantee hereunder shall be unconditional, irrespective of the validity, regularity or enforceability of the Notes or this Indenture, the absence of any action to enforce the same, any waiver or consent by any Holder of the Notes with respect to any thereof, the entry of any judgment against the Company, any action to enforce the same or any other circumstance which might otherwise constitute a legal or equitable discharge or defense of such Guarantor. Each Guarantor hereby waives and relinquishes: (i) any right to require the Trustee, the Holders or the Company (each, a "**Benefited Party**") to proceed against the Company or any other Person or to proceed against or exhaust any security held by a Benefited Party at any time or to pursue any other remedy in any secured party's power before proceeding against such Guarantor; (ii) any defense that may arise by reason of the incapacity, lack of authority, death or disability of any other Person or Persons or the failure of a Benefited Party to file or enforce a claim against the estate (in administration, bankruptcy or any other proceeding) of any other Person or Persons; (iii) demand, protest and notice of any kind (except as expressly required by this Indenture), including but not limited to notice of the existence, creation or incurring of any new or additional indebtedness or obligation or of any action or non-action on the part of such Guarantor, the Company, any Benefited Party, any creditor of such Guarantor or the Company or on the part of any other Person whomsoever in connection with any obligations the performance of which are hereby guaranteed; (iv) any defense based upon an election of remedies by a Benefited Party, including but not limited to an election to proceed against such Guarantor for reimbursement; (v) any defense based upon any statute or rule of law which provides that the obligation of a surety must be neither larger in amount nor in other respects more burdensome than that of the principal; (vi) any defense arising because of a Benefited Party's election, in any proceeding instituted under Bankruptcy Law, of the application of Section 1111(b)(2) of the Bankruptcy Code or any similar provision (including under Bermudan or Irish law); and (vii) any defense based on any borrowing or grant of a security interest under Section 364 of the Bankruptcy Code or any similar provision (including under Bermudan or Irish law). Each Guarantor hereby covenants that, except as otherwise provided therein, the Guarantee shall not be discharged except by payment or satisfaction, as the case may be, in full of all Guarantee Obligations, including principal and interest on the Notes and any other costs provided for under this Indenture (including as provided in Article 7).

(c) Each Guarantor as principal obligor and as a separate and independent obligation and liability from its other obligations and liabilities under this Indenture agrees to indemnify and keep indemnified each Holder and the Trustee in full and on demand in respect of the performance and discharge of the Guarantee Obligations (except where the Company's failure to perform or discharge the Guarantee Obligations results from such Holder's failure to comply with its obligations under the Indenture or the Trustee's negligence or willful misconduct or the Company contesting any payment or part of a payment in good faith).

(d) If any Holder or the Trustee is required by any court or otherwise to return to either the Company or any Guarantor, or any trustee or similar official acting in relation to either the Company or such Guarantor, any amount paid by the Company or such Guarantor to the Trustee or such Holder, then the Guarantee, to the extent theretofore discharged, shall be reinstated in full force and effect. Each Guarantor agrees that it shall not be entitled to any right of subrogation in relation to the Holders in respect of any Guarantee Obligations hereby until payment in full of all such obligations guaranteed hereby. Each Guarantor agrees that, as between it, on the one hand, and the Holders and the Trustee, on the other hand, (x) the maturity of the obligations guaranteed hereby may be accelerated as provided in Article 6 hereof for the purposes hereof, notwithstanding any stay, injunction or other prohibition preventing such acceleration in respect of the Guarantee Obligations, and (y) in the event of any acceleration of such obligations as provided in Article 6 hereof, such Guarantee Obligations (whether or not due and payable) shall forthwith become due and payable by such Guarantor for the purpose of the Guarantee.

(e) The Company and the Guarantors acknowledge that the allotment and issue of Ordinary Shares (whether upon exchange, under the terms of the Guarantee or otherwise) by Iterum will create an equivalent debt owing from the Company to Iterum. For the avoidance of doubt, upon Iterum's causing the delivery of Ordinary Shares in respect of the Exchange Obligation, the portion of such obligation consisting of an obligation to deliver or cause to be delivered Ordinary Shares shall be deemed satisfied to the extent of the shares so delivered.

(f) The exercise by a Holder of a Note of the right to exchange that Note for Ordinary Shares (if any) in compliance with the provisions of this Indenture shall be deemed to constitute a demand for immediate repayment by each of the Company and the Guarantors of that Note.

(g) Notwithstanding anything in this Indenture to the contrary, (i) with respect to the Subsidiary Guarantors, the Guarantee Obligations only include obligations to make cash payments of amounts due in accordance with the terms of this Indenture and do not include the performance of any obligation by the Company or Iterum to issue or deliver the Notes or any Ordinary Shares; and (ii) with respect to the Subsidiary Guarantors, the Guarantee does not apply to any liability to the extent that it would result in the Guarantee constituting unlawful financial assistance within the meaning of section 82 the Irish Companies Act 2014 (as amended).

Section 13.02 *Limitation of the Guarantors' Liability; Certain Bankruptcy Events*.

(a) Each Guarantor, and by its acceptance hereof each Holder, hereby confirms that it is the intention of all such parties that the Guarantee Obligations of the Guarantors pursuant to its Guarantee not constitute a fraudulent transfer or conveyance for purposes of any Bankruptcy Law, the Uniform Fraudulent Conveyance Act, the Uniform Fraudulent Transfer Act or any similar federal, state or foreign law. To effectuate the foregoing intention, the Holders and the Guarantors hereby irrevocably agree that the Guarantee Obligations of the Guarantors under this Article 13 shall be limited to the maximum amount as shall, after giving effect to all other contingent and fixed liabilities of the Guarantors, result in the Guarantee Obligations of the Guarantors under the Guarantee not constituting a fraudulent transfer or conveyance.

(b) Each Guarantor hereby covenants and agrees, to the fullest extent that it may do so under applicable law, that in the event of the insolvency, examinership, bankruptcy, dissolution, liquidation or reorganization of the Company, such Guarantor shall not file (or join in any filing of), or otherwise seek to participate in the filing of, any motion or request seeking to stay or to prohibit (even temporarily) execution on the Guarantee and hereby waives and agrees not to take the benefit of any such stay of execution, whether under Section 362 or 105 of the Bankruptcy Code or otherwise.

Section 13.03 *Execution And Delivery*. The Guarantee shall be evidenced by the execution and delivery of this Indenture or a supplement to this Indenture and no notation of the Guarantee need be endorsed on any Note. Each Guarantor hereby agrees that its Guarantee set forth in Section 13.01 shall remain in full force and effect notwithstanding the absence of the endorsement of any notation of such Guarantee on the Notes. If an Officer whose signature is on this Indenture no longer holds that office at the time the Trustee authenticates the Note, the Guarantee shall be valid nevertheless. The delivery of any Note by the Trustee, after the authentication thereof hereunder, shall constitute due delivery of the Guarantee set forth in this Indenture on behalf of the Guarantors.

ARTICLE 14
Exchange of Notes

Section 14.01 *Exchange.*

(a) *Exchange Privilege*. Subject to and upon compliance with the provisions of this Article 14, each Holder of a Note shall have the right, at such Holder's option, to exchange all or any portion (if the portion to be exchanged is a minimum of $1,000 principal amount or a multiple of $1,000 in excess thereof) of the then-outstanding portion of such Note (including the accrued but unpaid interest thereon) on or after January 21, 2021 and prior to the earlier of (i) the close of business on the Scheduled Trading Day immediately preceding delivery of a Mandatory Exchange Notice and (ii) the close of business on the second Scheduled Trading Day immediately preceding the Interest Record Date, in each case, at an initial exchange rate of 1,000

Ordinary Shares (subject to adjustment as provided in this Article 14, the "**Exchange Rate**") per $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged. Any accrued and unpaid interest being exchanged under this Section 14.01(a) or Section 14.01(b), shall be calculated to include all interest accrued on the Notes being exchanged to, but excluding, the Exchange Settlement Date.

(b) *Mandatory Exchange*. Subject to the provisions of this Article 14, the Notes shall be automatically exchanged at the Exchange Rate following the occurrence of the Mandatory Exchange Trigger Event (the "**Mandatory Exchange**"). No later than three Business Days following the occurrence of the Mandatory Exchange Trigger Event, the Company shall or, at its written request received by the Trustee, the Trustee, in the name of and at the expense of the Company, shall deliver or cause to be delivered a notice of such Mandatory Exchange (a "**Mandatory Exchange Notice**") to the Exchange Agent (if other than the Trustee) and the Holders; *provided*, *however*, that, if the Company shall give such notice, it shall also give written notice of the Mandatory Exchange to the Trustee (if the Trustee is not the Exchange Agent). The Mandatory Exchange Notice shall (i) state that the Mandatory Exchange Trigger Event has occurred, (ii) state the current Exchange Rate and the Settlement Method for the Mandatory Exchange as elected by the Company (and, in the case of an election of Combination Settlement, the Specified Dollar Amount per $1,000 principal amount of Notes) and (iii) include the Exchange Date for the Mandatory Exchange, which shall be the tenth Business Day following the date of such notice.

Following delivery of the Mandatory Exchange Notice, each Holder shall follow the procedure described in Section 14.02(b), and the Company shall have no obligation to issue the exchange consideration unless such Holder has complied with the provisions thereof.

On or prior to the Exchange Date for the Mandatory Exchange, the Company shall deliver an Officer's Certificate to the Trustee and the Exchange Agent (if other than the Trustee), stating that the Mandatory Exchange Trigger Event has occurred.

Subject to Section 14.02 and Section 14.07(a), upon exchange of any Note pursuant to this Section 14.01(b), the Company shall pay or deliver, as the case may be, to each exchanging Holder the consideration due to such Holder in accordance with Section 14.02(a).

(c) *Ownership Caps*.

(i) Notwithstanding anything herein to the contrary, Iterum shall not issue to any Holder of a Specified Note, and no Holder of a Specified Note may acquire, a number of Ordinary Shares upon exchange of a Note and the Company shall not otherwise deliver any Ordinary Shares pursuant hereto, to the extent that, (1) upon such exchange, the number of Ordinary Shares then beneficially owned by the Holder and its Affiliates and any other Persons or entities whose beneficial ownership of Ordinary Shares would be aggregated with the Holder's for purposes of Section 13(d) of the

Exchange Act (including any shares held by any "group" of which the Holder is a member, but excluding shares beneficially owned by virtue of the ownership of securities or rights to acquire securities that have limitations on the right to exchange, convert, exercise or purchase similar to the limitation set forth herein) would exceed 19.99% of the total number of Ordinary Shares issued and outstanding or (2) such issuance, when aggregated with any other Ordinary Shares theretofore or simultaneously therewith issued to or otherwise beneficially owned by the Holder and its Affiliates and any other Persons or entities whose beneficial ownership of Ordinary Shares would be aggregated with the Holder's for purposes of Section 13(d) of the Exchange Act (including any shares held by any "group" of which the Holder is a member, but excluding shares beneficially owned by virtue of the ownership of securities or rights to acquire securities that have limitations on the right to exchange, convert, exercise or purchase similar to the limitation set forth herein) would otherwise result in a "change of control" of Iterum within the meaning of Nasdaq Listing Rule 5635(b) ((a) and (b), together, the "**Individual Ownership Cap**"); except that such limitation shall not apply in the event that Iterum obtains all necessary Shareholder Approvals for such exchange. For purposes hereof, "group" has the meaning set forth in Section 13(d) of the Exchange Act and applicable regulations of the Commission, and the percentage held by the Holder shall be determined in a manner consistent with the provisions of Section 13(d) of the Exchange Act.

(ii) Notwithstanding anything herein to the contrary, Iterum shall not issue to any Holder of a Specified Note, and no such Holder may acquire, a number of Ordinary Shares upon exchange of a Note and the Company shall not otherwise deliver any Ordinary Shares pursuant hereto, to the extent that the issuance of such Ordinary Shares would, together with any other issuance of Ordinary Shares by Iterum to any Holders of Specified Notes upon the exchange of all Specified Notes, exceed 19.99% of the issued and outstanding Ordinary Shares immediately prior to the initial issuance of the Specified Notes (the "**Aggregate Ownership Cap**"), except that such limitation shall not apply in the event that Iterum (a) obtains all necessary Shareholder Approvals for the issuances of Ordinary Shares in excess of the Aggregate Ownership Cap or (b) obtains a waiver from the Nasdaq Stock Market LLC of all applicable listing rules requiring such stockholder approval. Until one of the exceptions in clauses (a) or (b) of the proceeding sentence applies and has been satisfied, upon exchange of a Specified Note the Holder thereof shall in no event, subject to the terms of Section 14.01 and Section 14.02, be entitled to receive a number of Ordinary Shares (determined in the aggregate for all such exchanges of a Specified Note by such Holder) in excess of (x) 14,868,973 (subject to adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization) multiplied by (y) the quotient obtained by dividing the principal amount of such Specified Note by the initial aggregate principal of all Specified Notes immediately following their original issuance.

(iii) Notwithstanding anything herein to the contrary, Iterum shall not issue to any Holder of a Specified Note, and no such Holder may acquire, a number of Ordinary Shares upon exchange of a Note and the Company shall not otherwise deliver any Ordinary Shares pursuant hereto, to the extent that the issuance of such Ordinary Shares would, together with any other issuance of Ordinary Shares by Iterum to any Holders of Specified Notes upon the exchange of all Specified Notes, exceed the Available Shares (the "**Available Shares Ownership Cap**"), except that such limitation shall not apply in the event that Iterum obtains the Authorized Shares Approval. Until the exception in the proceeding sentence applies and has been satisfied , upon exchange of a Specified Note the Holder thereof shall in no event, subject to the terms of Section 14.01 and Section 14.02, be entitled to receive a number of Ordinary Shares (determined in the aggregate for all such exchanges of a Specified Note by such Holder) in excess of (x) the Available Shares multiplied by (y) the quotient obtained by dividing the principal amount of such Specified Note by the initial aggregate principal of all Specified Notes immediately following their original issuance.

(iv) Notwithstanding anything herein to the contrary, if the Company shall have chosen Physical Settlement or Combination Settlement pursuant to Section 14.02(a) and the exchange of a Note would otherwise result in its Holder exceeding the Individual Ownership Cap, the Aggregate Ownership Cap or the Available Shares Ownership Cap, such that the number of shares issuable upon exchange of such Note is limited by Section 14.01(c)(i), Section 14.01(c)(ii) or Section 14.01(c)(iii), the applicable portion of the Note that is not exchanged as result of such limitations shall remain outstanding in accordance with the terms of this Indenture and the obligation of Iterum to exchange such Note and issue the shares that would have resulted in the Holder exceeding the Individual Ownership Cap, the Aggregate Ownership Cap or the Available Shares Ownership Cap shall not be extinguished, and Iterum and the Trustee shall as promptly as practicable exchange such Notes and deliver to the Holder such number of shares that would have resulted in the Holder exceeding the Individual Ownership Cap, the Aggregate Ownership Cap or the Available Shares Ownership Cap following such time as the issuance of such shares would not exceed the Individual Ownership Cap, the Aggregate Ownership Cap or the Available Shares Ownership Cap; provided, however, that in the case of an issuance of shares that would result in the Holder exceeding the Individual Ownership Cap, such Holder shall provide written notice to the Company, Iterum and the Trustee that such delivery would not result in the Holder exceeding the Individual Ownership Cap and shall provide the Company, Iterum and the Trustee with any certifications, representations and other documentation reasonably requested by the Company, Iterum or the Trustee in connection therewith. In no event shall the Company nor the Guarantors have any obligation to pay to the Holder in cash the value of the Ordinary Shares that would otherwise be issuable upon an exchange in the absence of the Individual Ownership Cap, the Aggregate Ownership Cap or the Available Shares

Ownership Cap; provided that any Note not so exchanged as a result of the application of the foregoing shall remain outstanding in accordance with the terms of this Indenture.

(v) Notwithstanding anything herein to the contrary, in the event a Holder of a Physical Note (a) notifies the Company, Iterum and the Trustee after delivery of a Mandatory Exchange Notice including the Company's election of Physical Settlement or Combination Settlement and prior to completion of the Mandatory Exchange that such Holder would be obligated to make a mandatory offer for the entire issued share capital of Iterum pursuant to Rule 9 of the Irish Takeover Rules as a result of the issuance of Ordinary Shares to the Holder upon a Mandatory Exchange and (b) provides the Company, Iterum and the Trustee with any certifications, representations and other documentation reasonably requested by the Company, Iterum or the Trustee in connection therewith, Iterum shall issue to such Holder the maximum number of Ordinary Shares that may be issued to such Holder without obligating such Holder to make such a mandatory offer and shall not exchange Ordinary Shares for the remaining portion of such Note; provided, however, that the obligation of Iterum to issue any such additional Ordinary Shares shall not be extinguished, and Iterum shall make such delivery as promptly as practicable after any such Holder gives notice to the Company, Iterum and the Trustee that such delivery would not result in the Holder being obligated to make a mandatory offer for the entire issued share capital of Iterum pursuant to Rule 9 of the Irish Takeover Rules.

(vi) Notwithstanding anything herein to the contrary, in the event a Beneficial Holder (a) notifies the Company, Iterum and the Trustee after delivery of a Mandatory Exchange Notice including the Company's election of Physical Settlement or Combination Settlement and prior to completion of the Mandatory Exchange that such Beneficial Holder would be obligated to make a mandatory offer for the entire issued share capital of Iterum pursuant to Rule 9 of the Irish Takeover Rules as a result of the issuance of Ordinary Shares to the Beneficial Holder upon a Mandatory Exchange, (b) provides the Company, Iterum and the Trustee with any certifications, representations and other documentation reasonably requested by the Company, Iterum or the Trustee in connection therewith and (c) requests a Physical Note in lieu of a beneficial interest in a Global Note, the Company shall promptly cause a Physical Note to be issued to the Beneficial Holder in accordance with Section 2.05(c), and shall treat such Beneficial Holder as though such Beneficial Holder were a Holder who had delivered a notice pursuant to Section 14.01(c)(v).

(vii) For the avoidance of doubt, any Notes or portion thereof not exchanged for Ordinary Shares as result of the provisions of this Section 14.01(c) shall continue to be held by the Holders thereof, and none of the rights, obligations and other terms under the Notes, this Indenture or the Guarantee with respect to such Notes shall be deemed amended or otherwise modified in connection with such exchange.

(viii) Any Ordinary Shares issued upon exchange of a Specified Note shall not be voted in connection with, or counted in support of, the Shareholder Approval.

Section 14.02 *Exchange Procedure; Settlement Upon Exchange.*

(a) Subject to Section 14.01(c), this Section 14.02 and Section 14.07(a), upon exchange of any Note, the Company shall, at its election, pay or deliver, as the case may be, to the exchanging Holder, in respect of each $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged, cash ("**Cash Settlement**"), Ordinary Shares, together with cash, if applicable, in lieu of delivering any fractional Ordinary Share in accordance with subsection (i) of this Section 14.02 ("**Physical Settlement**") or a combination of cash and Ordinary Shares, together with cash, if applicable, in lieu of delivering any fractional Ordinary Share in accordance with subsection (i) of this Section 14.02 ("**Combination Settlement**"), as set forth in this Section 14.02.

(i) All exchanges for which the relevant Exchange Date occurs after the Company's issuance of a Redemption Notice with respect to the Notes and prior to the close of business on the second Scheduled Trading Day immediately preceding the related Redemption Date, and all exchanges for which the relevant Exchange Date occurs on or after October 31, 2024, shall be settled using the same Settlement Method.

(ii) Except for any exchanges for which the relevant Exchange Date occurs after the Company's issuance of a Redemption Notice with respect to the Notes but prior to the close of business on the second Scheduled Trading Day immediately preceding the related Redemption Date, and any exchanges for which the relevant Exchange Date occurs on or after October 31, 2024, the Company shall use the same Settlement Method for all exchanges with the same Exchange Date, but the Company shall not have any obligation to use the same Settlement Method with respect to exchanges that occur on different Exchange Dates.

(iii) If, in respect of any Exchange Date (or the period described in the fourth immediately succeeding set of parentheses, as the case may be), the Company elects to deliver a written notice (the "**Settlement Notice**") of the relevant Settlement Method in respect of such Exchange Date (or such period, as the case may be), the Company shall deliver such Settlement Notice to exchanging Holders (with a copy to the Trustee and Exchange Agent) no later than the close of business on the Trading Day immediately following the relevant Exchange Date (or, in the case of any exchanges of any Notes for which the relevant Exchange Date occurs (A) on or after the date of issuance of a Redemption Notice with respect to the Notes and prior to the close of business on the second Scheduled Trading Day immediately preceding the related Redemption Date in such Redemption Notice or (B) on or after October 31, 2024, no later than the close of business on the Business Day immediately preceding October 31, 2024); *provided,*

however, that with respect to a Mandatory Exchange, the Mandatory Exchange Notice shall constitute the Settlement Notice. If the Company does not elect a Settlement Method prior to the deadline set forth in the immediately preceding sentence, the Company shall no longer have the right to elect Cash Settlement or Physical Settlement and the Company shall be deemed to have elected Combination Settlement in respect of its Exchange Obligation, and the Specified Dollar Amount per $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged shall be equal to $1,000. Such Settlement Notice shall specify the relevant Settlement Method and in the case of an election of Combination Settlement, the relevant Settlement Notice shall indicate the Specified Dollar Amount per $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged. If the Company delivers a Settlement Notice electing Combination Settlement in respect of its Exchange Obligation but does not indicate a Specified Dollar Amount per $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged in such Settlement Notice, the Specified Dollar Amount per $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged shall be deemed to be $1,000.

(iv) The cash, Ordinary Shares or combination of cash and Ordinary Shares in respect of any exchange of Notes (the "**Settlement Amount**") shall be computed as follows:

(A) if the Company elects to satisfy its Exchange Obligation in respect of such exchange by Physical Settlement, the Company shall cause to be delivered to the exchanging Holder in respect of each $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged a number of Ordinary Shares equal to the Exchange Rate in effect on the Exchange Date;

(B) if the Company elects to satisfy its Exchange Obligation in respect of such exchange by Cash Settlement, the Company shall pay to the exchanging Holder in respect of each $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged cash in an amount equal to the sum of the Daily Exchange Values for each of the 30 consecutive Trading Days during the related Observation Period; and

(C) if the Company elects (or is deemed to have elected) to satisfy its Exchange Obligation in respect of such exchange by Combination Settlement, the Company shall pay or cause to be delivered, as the case may be, in respect of each $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged, a Settlement Amount equal to the sum of the Daily Settlement Amounts for each of the 30 consecutive Trading Days during the related Observation Period.

(v) The Daily Settlement Amounts (if applicable) and the Daily Exchange Values (if applicable) shall be determined by the Company promptly following the last day of the Observation Period. Promptly after such determination of the Daily Settlement Amounts or the Daily Exchange Values, as the case may be, and the amount of cash payable in lieu of delivering any fractional Ordinary Share, the Company shall notify the Trustee and the Exchange Agent (if other than the Trustee) of the Daily Settlement Amounts or the Daily Exchange Values, as the case may be, and the amount of cash payable in lieu of delivering fractional Ordinary Shares. The Trustee and the Exchange Agent (if other than the Trustee) shall have no responsibility for any such determination.

(b) Subject to Section 14.02(e), before any Holder of a Note shall be entitled to exchange a Note as set forth above, such Holder shall (i) in the case of a Global Note, comply with the procedures of the Depositary in effect at that time and (ii) in the case of a Physical Note (1) complete, manually sign and deliver an irrevocable notice to the Exchange Agent as set forth in the Form of Notice of Exchange (or a facsimile thereof) (a "**Notice of Exchange**") at the Corporate Trust Office or the office of the Exchange Agent (if other than the Trustee) and state in writing therein the principal amount of Notes to be exchanged and the name or names (with addresses) in which such Holder wishes the certificate or certificates for any Ordinary Shares to be delivered upon settlement of the Exchange Obligation to be registered, (2) surrender such Notes, duly endorsed to the Company or in blank (and accompanied by appropriate endorsement and transfer documents), at the Corporate Trust Office or the office of the Exchange Agent (if other than the Trustee), (3) if required, furnish appropriate endorsements and transfer documents and (4) with respect to any exchange by a Holder of a Specified Note, provide the Company, Iterum and the Trustee with any certifications, representations and other documentation reasonably requested by the Company, Iterum or the Trustee to demonstrate the Holder's compliance with Section 14.01(c); *provided, however*, that the Notice of Exchange in clause (1) shall not be required in the case of a Mandatory Exchange. The Trustee (and, if different, the Exchange Agent) shall notify the Company of any voluntary exchange pursuant to this Article 14 on the Exchange Date for such exchange. No Notice of Exchange with respect to any Notes may be surrendered by a Holder thereof if (i) such Holder has also delivered a Fundamental Change Repurchase Notice to the Company in respect of such Notes and has not validly withdrawn such Fundamental Change Repurchase Notice in accordance with Section 15.03 or (ii) the Company has delivered a Mandatory Exchange Notice.

If more than one Note shall be surrendered for exchange at one time by the same Holder, the Exchange Obligation with respect to such Notes shall be computed on the basis of the aggregate of principal of and accrued but unpaid interest on the Notes so surrendered (or specified portions thereof to the extent permitted thereby).

(c) A Note shall be deemed to have been exchanged immediately prior to the close of business on the date (the "**Exchange Date**") that the Holder has complied with the requirements set forth in subsection (b) above (or, in the case of a Mandatory Exchange, the Exchange Date

set forth in the Mandatory Exchange Notice). Except as provided in Section 14.07(a), the Company shall pay or cause to be delivered, as the case may be, the consideration due in respect of the Exchange Obligation (i) on the second Business Day immediately following the relevant Exchange Date, if the Company elects to use Physical Settlement, or (ii) on the second Business Day immediately following the last Trading Day of the relevant Observation Period, in the case of any other Settlement Method (the "**Exchange Settlement Date**"). Subject to Section 14.01(c), if any Ordinary Shares are due to exchanging Holders, the Company shall issue or cause to be issued, and deliver to the Exchange Agent or to such Holder, or such Holder's nominee or nominees, certificates or a book-entry transfer through the Depositary for the full number of Ordinary Shares to which such Holder shall be entitled in satisfaction of the Company's Exchange Obligation.

(d) In case any Note shall be surrendered for partial exchange, the Company shall execute and the Trustee shall authenticate and deliver to or upon the written order of the Holder of the Note so surrendered a new Note or Notes in authorized denominations in an aggregate principal amount equal to the unexchanged portion of the surrendered Note, without payment of any service charge by the exchanging Holder but, if required by the Company or Trustee, with payment of a sum sufficient to cover any documentary, stamp or similar issue or transfer tax or similar governmental charge required by law or that may be imposed in connection therewith as a result of the name of the Holder of the new Notes issued upon such exchange being different from the name of the Holder of the old Notes surrendered for such exchange.

(e) If a Holder submits a Note for exchange, the Company shall pay any documentary, stamp or similar issue or transfer tax due on the issuance of any Ordinary Shares upon exchange, unless the tax is due because the Holder requests such shares to be issued in a name other than the Holder's name, in which case the Holder shall pay that tax. The Exchange Agent may refuse to deliver the certificates representing the Ordinary Shares being issued in a name other than the Holder's name until the Trustee receives a sum sufficient to pay any tax that is due by such Holder in accordance with the immediately preceding sentence.

(f) Upon the exchange of an interest in a Global Note, the Trustee, or the Custodian at the direction of the Trustee, shall make a notation on such Global Note as to the reduction in the principal amount represented thereby. The Company shall notify the Trustee in writing of any exchange of Notes effected through any Exchange Agent other than the Trustee.

(g) Upon exchange, a Holder shall not receive any separate cash payment for accrued and unpaid interest, if any. The Company's settlement of the full Exchange Obligation shall be deemed to satisfy in full its obligation to pay the principal amount of the Note and accrued and unpaid interest, if any, to, but not including, the relevant Exchange Date. As a result, accrued and unpaid interest, if any, to, but not including, the relevant Exchange Date shall be deemed to be paid in full rather than canceled, extinguished or forfeited. Upon an exchange of Notes for a

combination of cash and Ordinary Shares, any accrued and unpaid interest will be deemed to be paid first out of the cash paid upon such exchange.

(h) The Person in whose name the certificate for any Ordinary Shares delivered upon exchange is registered shall be treated as a shareholder of record as of the close of business on the relevant Exchange Date (if the exchange is settled by Physical Settlement) or the last Trading Day of the relevant Observation Period (if the Company elects to satisfy the related Exchange Obligation by Combination Settlement), as the case may be. Upon an exchange of Notes, such Person shall no longer be a Holder of such Notes surrendered for exchange.

(i) The Company shall not issue any fractional Ordinary Share upon exchange of the Notes and shall instead pay cash in lieu of delivering any fractional Ordinary Share issuable upon exchange based on the Daily VWAP on the relevant Exchange Date (in the case of Physical Settlement) or based on the Daily VWAP on the last Trading Day of the relevant Observation Period (in the case of Combination Settlement). For each Note surrendered for exchange, if the Company has elected (or is deemed to have elected) Combination Settlement, the full number of shares that shall be issued upon exchange thereof shall be computed on the basis of the aggregate Daily Settlement Amounts for the relevant Observation Period and any fractional shares remaining after such computation shall be paid in cash.

Section 14.03 *Intentionally Omitted.*

Section 14.04 *Adjustment of Exchange Rate.* The Exchange Rate shall be adjusted from time to time by the Company if any of the following events occurs, except that the Company shall not make any adjustments to the Exchange Rate if Holders of the Notes participate (other than in the case of (x) a share split or share combination or (y) a tender or exchange offer), at the same time and upon the same terms as holders of the Ordinary Shares and solely as a result of holding the Notes, in any of the transactions described in this Section 14.04, without having to exchange their Notes, as if they held a number of Ordinary Shares equal to the Exchange Rate per each $1,000 of principal of and accrued but unpaid interest on the Notes held by such Holder.

(a) If Iterum exclusively issues Ordinary Shares as a dividend or distribution on Ordinary Shares, or if Iterum effects a share split or share combination, the Exchange Rate shall be adjusted based on the following formula:

$$CR' = CR_0 \times \frac{OS'}{OS_0}$$

where,

CR_0 =the Exchange Rate in effect immediately prior to the open of business on the Ex-Dividend Date of such dividend or distribution, or immediately prior to the open of

business on the Effective Date of such share split or share combination, as applicable;

CR' =the Exchange Rate in effect immediately after the open of business on such Ex-Dividend Date or Effective Date;

OS_0 =the number of Ordinary Shares outstanding immediately prior to the open of business on such Ex-Dividend Date or Effective Date (before giving effect to any such dividend, distribution, split or combination); and

OS' =the number of Ordinary Shares outstanding immediately after giving effect to such dividend, distribution, share split or share combination.

Any adjustment made under this Section 14.04(a) shall become effective immediately after the open of business on the Ex-Dividend Date for such dividend or distribution, or immediately after the open of business on the Effective Date for such share split or share combination, as applicable. If any dividend or distribution of the type described in this Section 14.04(a) is declared but not so paid or made, or any share split or combination of the type described in this Section 14.04(a) is announced but the outstanding Ordinary Shares are not split or combined, as the case may be, the Exchange Rate shall be immediately readjusted, effective as of the date Iterum's Board of Directors determines not to pay such dividend or distribution, or not to split or combine the outstanding Ordinary Shares, as the case may be, to the Exchange Rate that would then be in effect if such dividend or distribution had not been declared or such share split or combination had not been announced.

(b) If Iterum issues to all or substantially all holders of the Ordinary Shares any rights, options or warrants (other than a Rights Offering) entitling them, for a period of not more than 45 calendar days after the announcement date of such issuance, to subscribe for or purchase Ordinary Shares at a price per share that is less than the average of the Last Reported Sale Prices of the Ordinary Shares for the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the date of announcement of such issuance, the Exchange Rate shall be increased based on the following formula:

$$CR' = CR_0 \times \frac{OS_0 + X}{OS_0 + Y}$$

where,

CR_0 =the Exchange Rate in effect immediately prior to the open of business on the Ex-Dividend Date for such issuance;

CR' =the Exchange Rate in effect immediately after the open of business on such Ex-Dividend Date;

OS_0 =the number of Ordinary Shares outstanding immediately prior to the open of business on such Ex-Dividend Date;

X =the total number of Ordinary Shares issuable pursuant to such rights, options or warrants; and

Y =the number of Ordinary Shares equal to the aggregate price payable to exercise such rights, options or warrants, *divided by* the average of the Last Reported Sale Price per Ordinary Share over the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the date of announcement of the issuance of such rights, options or warrants.

Any increase made under this Section 14.04(b) shall be made successively whenever any such rights, options or warrants are issued and shall become effective immediately after the open of business on the Ex-Dividend Date for such issuance. To the extent that Ordinary Shares are not delivered after the expiration of such rights, options or warrants, the Exchange Rate shall be decreased to the Exchange Rate that would then be in effect had the increase with respect to the issuance of such rights, options or warrants been made on the basis of delivery of only the number of Ordinary Shares actually delivered. If such rights, options or warrants are not so issued, the Exchange Rate shall be decreased to the Exchange Rate that would then be in effect if such Ex-Dividend Date for such issuance had not occurred. For the avoidance of doubt, if the application of the foregoing formula would result in a decrease in the Exchange Rate, no adjustment to the Exchange Rate will be made (other than with respect to the Company's right to readjust the Exchange Rate).

For purposes of this Section 14.04(b), in determining whether any rights, options or warrants entitle the holders of the Ordinary Shares to subscribe for or purchase Ordinary Shares at less than such average of the Last Reported Sale Price per Ordinary Share for the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the date of announcement for such issuance, and in determining the aggregate offering price of such Ordinary Shares, there shall be taken into account any consideration received by Iterum for such rights, options or warrants and any amount payable on exercise or conversion thereof, the value of such consideration, if other than cash, to be determined by Iterum's Board of Directors in good faith.

(c) If Iterum distributes shares of its Capital Stock, evidences of its indebtedness, other assets or property of Iterum or rights, options or warrants to subscribe for, purchase or otherwise acquire its Capital Stock or other securities of Iterum, to all or substantially all holders of the Ordinary Shares, excluding (i) dividends, distributions or issuances as to which an adjustment was effected pursuant to Section 14.04(a) or Section 14.04(b), (ii) dividends or

distributions paid exclusively in cash as to which the provisions set forth in Section 14.04(d) shall apply, (iii) distributions of Reference Property in a transaction described in Section 14.07, (iv) Spin-Offs as to which the provisions set forth below in this Section 14.04(c) shall apply or (v) a Rights Offering (any of such shares of Capital Stock, evidences of indebtedness, other assets or property orrights, options or warrants to subscribe for, purchase or otherwise acquire Capital Stock or other securities, the "**Distributed Property**"), then the Exchange Rate shall be increased based on the following formula:

$$CR' = CR_0 \times \frac{SP_0}{SP_0 - FMV}$$

where,

CR_0	=the Exchange Rate in effect immediately prior to the open of business on the Ex-Dividend Date for such distribution;
CR'	=the Exchange Rate in effect immediately after the open of business on such Ex-Dividend Date;
SP_0	=the average of the Last Reported Sale Price per Ordinary Share over the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the Ex-Dividend Date for such distribution; and
FMV	=the fair market value (as determined by Iterum's Board of Directors in good faith) of the Distributed Property with respect to each outstanding Ordinary Share on the Ex-Dividend Date for such distribution.

Any increase made under the portion of this Section 14.04(c) above shall become effective immediately after the open of business on the Ex-Dividend Date for such distribution. If such distribution is not so paid or made, the Exchange Rate shall be decreased to the Exchange Rate that would then be in effect if such distribution had not been declared. For the avoidance of doubt, if the application of the foregoing formula would result in a decrease in the Exchange Rate, no adjustment to the Exchange Rate will be made (other than with respect to the Company's right to readjust the Exchange Rate).

Notwithstanding the foregoing, if "FMV" (as defined above) is equal to or greater than "SP_0" (as defined above), in lieu of the foregoing increase, each Holder of a Note shall receive, in respect of each $1,000 of principal of and accrued but unpaid interest on the Notes held by such Holder, at the same time and upon the same terms as holders of the Ordinary Shares receive the Distributed Property, the amount and kind of Distributed Property such Holder would have received if such Holder owned a number of Ordinary Shares equal to the Exchange Rate in effect on the Ex-Dividend Date for the distribution. If the Board of Directors determines the "FMV"

(as defined above) of any distribution for purposes of this Section 14.04(c) by reference to the actual or when-issued trading market for any securities, it shall in doing so consider the prices in such market over the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the Ex-Dividend Date for such distribution.

With respect to an adjustment pursuant to this Section 14.04(c) where there has been a payment of a dividend or other distribution on the Ordinary Shares of shares of Capital Stock of any class or series, or similar equity interest, of or relating to a Subsidiary or other business unit of Iterum, that are, or, when issued, will be, listed or admitted for trading on a U.S. national securities exchange (a "**Spin-Off**"), the Exchange Rate shall be increased based on the following formula:

$$CR' = CR_0 \times \frac{FMV_0 + MP_0}{MP_0}$$

where,

CR_0	=the Exchange Rate in effect immediately prior to the end of the Valuation Period;
CR'	=the Exchange Rate in effect immediately after the end of the Valuation Period;
FMV_0	=the average of the Last Reported Sale Price per share or unit of the Capital Stock or similar equity interest distributed to holders of the Ordinary Shares applicable to one Ordinary Share (determined by reference to the definition of Last Reported Sale Price as set forth in Section 1.01 as if references therein to Ordinary Shares were to such Capital Stock or similar equity interest) over the first 10 consecutive Trading Day period beginning on, and including, the Ex-Dividend Date of the Spin-Off (the "**Valuation Period**"); and
MP_0	=the average of the Last Reported Sale Price per Ordinary Share over the Valuation Period.

The increase to the Exchange Rate under the preceding paragraph shall occur at the close of business on the last Trading Day of the Valuation Period; *provided* that (i) in respect of any exchange of Notes for which Physical Settlement is applicable, if the relevant Exchange Date occurs during the Valuation Period, the reference to "10" in the portion of this Section 14.04(c) related to Spin-Offs shall be deemed replaced with such lesser number of Trading Days as have elapsed from, and including, the Ex-Dividend Date for such Spin-Off to, and including, such Exchange Date in determining the Exchange Rate and (ii) in respect of any exchange of Notes for which Cash Settlement or Combination Settlement is applicable, for any Trading Day that falls within the relevant Observation Period for such exchange and within the Valuation Period, the reference to "10" in this Section 14.04(c) related to Spin-Offs shall be deemed replaced with

such lesser number of Trading Days as have elapsed from, and including, the Ex-Dividend Date for such Spin-Off to, and including, such Trading Day in the relevant Observation Period for purposes of determining the Exchange Rate as of such Trading Day. For the avoidance of doubt, if the application of the foregoing formula would result in a decrease in the Exchange Rate, no adjustment to the Exchange Rate will be made (other than with respect to the Company's right to readjust the Exchange Rate).

For purposes of this Section 14.04(c) (and subject in all respect to Section 14.11), rights, options or warrants distributed by Iterum to all holders of the Ordinary Shares entitling them to subscribe for or purchase shares of Iterum's Capital Stock, including Ordinary Shares (either initially or under certain circumstances), which rights, options or warrants, until the occurrence of a specified event or events ("**Trigger Event**"): (i) are deemed to be transferred with such Ordinary Shares; (ii) are not exercisable; and (iii) are also issued in respect of future issuances of Ordinary Shares, shall be deemed not to have been distributed for purposes of this Section 14.04(c) (and no adjustment to the Exchange Rate under this Section 14.04(c) will be required) until the occurrence of the earliest Trigger Event, whereupon such rights, options or warrants shall be deemed to have been distributed and an appropriate adjustment (if any is required) to the Exchange Rate shall be made under this Section 14.04(c). If any such right, option or warrant, including any such existing rights, options or warrants distributed prior to the date of this Indenture, are subject to events, upon the occurrence of which such rights, options or warrants become exercisable to purchase different securities, evidences of indebtedness or other assets, then the date of the occurrence of any and each such event shall be deemed to be the date of distribution and Ex-Dividend Date with respect to new rights, options or warrants with such rights (in which case the existing rights, options or warrants shall be deemed to terminate and expire on such date without exercise by any of the holders thereof). In addition, in the event of any distribution (or deemed distribution) of rights, options or warrants, or any Trigger Event or other event (of the type described in the immediately preceding sentence) with respect thereto that was counted for purposes of calculating a distribution amount for which an adjustment to the Exchange Rate under this Section 14.04(c) was made, (1) in the case of any such rights, options or warrants that shall all have been redeemed or purchased without exercise by any holders thereof, upon such final redemption or purchase (x) the Exchange Rate shall be readjusted as if such rights, options or warrants had not been issued and (y) the Exchange Rate shall then again be readjusted to give effect to such distribution, deemed distribution or Trigger Event, as the case may be, as though it were a cash distribution, equal to the per share redemption or purchase price received by a holder or holders of Ordinary Shares with respect to such rights, options or warrants (assuming such holder had retained such rights, options or warrants), made to all holders of Ordinary Shares as of the date of such redemption or purchase, and (2) in the case of such rights, options or warrants that shall have expired or been terminated without exercise by any holders thereof, the Exchange Rate shall be readjusted as if such rights, options and warrants had not been issued.

For purposes of Section 14.04(a), Section 14.04(b) and this Section 14.04(c), if any dividend or distribution to which this Section 14.04(c) is applicable also includes one or both of:

(A) a dividend or distribution of Ordinary Shares to which Section 14.04(a) is applicable (the "**Clause A Distribution**"); or

(B) a dividend or distribution of rights, options or warrants to which Section 14.04(b) is applicable (the "**Clause B Distribution**"),

then, in either case, (1) such dividend or distribution, other than the Clause A Distribution and the Clause B Distribution, shall be deemed to be a dividend or distribution to which this Section 14.04(c) is applicable (the "**Clause C Distribution**") and any Exchange Rate adjustment required by this Section 14.04(c) with respect to such Clause C Distribution shall then be made, and (2) the Clause A Distribution and Clause B Distribution shall be deemed to immediately follow the Clause C Distribution and any Exchange Rate adjustment required by Section 14.04(a) and Section 14.04(b) with respect thereto shall then be made, except that, if determined by the Company (I) the "Ex-Dividend Date" of the Clause A Distribution and the Clause B Distribution shall be deemed to be the Ex-Dividend Date of the Clause C Distribution and (II) any Ordinary Shares included in the Clause A Distribution or Clause B Distribution shall be deemed not to be "outstanding immediately prior to the open of business on such Ex-Dividend Date or Effective Date" within the meaning of Section 14.04(a) or "outstanding immediately prior to the open of business on such Ex-Dividend Date" within the meaning of Section 14.04(b).

(d) If any cash dividend or distribution is made to all or substantially all holders of the Ordinary Shares, the Exchange Rate shall be adjusted based on the following formula:

$$CR' = CR_0 \times \frac{SP_0}{SP_0 - C}$$

where,

CR0 =the Exchange Rate in effect immediately prior to the open of business on the Ex-Dividend Date for such dividend or distribution;

CR' =the Exchange Rate in effect immediately after the open of business on the Ex-Dividend Date for such dividend or distribution;

SP0 =the Last Reported Sale Price per Ordinary Share on the Trading Day immediately preceding the Ex-Dividend Date for such dividend or distribution; and

C =the amount in cash per share the Company distributes to all or substantially all holders of the Ordinary Shares.

Any increase pursuant to this Section 14.04(d) shall become effective immediately after the open of business on the Ex-Dividend Date for such dividend or distribution. If such dividend or distribution is not so paid, the Exchange Rate shall be decreased, effective as of the date Iterum's Board of Directors determines not to make or pay such dividend or distribution, to be the Exchange Rate that would then be in effect if such dividend or distribution had not been declared. For the avoidance of doubt, if the application of the foregoing formula would result in a decrease in the Exchange Rate, no adjustment to the Exchange Rate will be made (other than with respect to the Company's right to readjust the Exchange Rate).

Notwithstanding the foregoing, if "C" (as defined above) is equal to or greater than "SP_0" (as defined above), in lieu of the foregoing increase, each Holder of a Note shall receive, for each $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged, at the same time and upon the same terms as holders of Ordinary Shares, the amount of cash that such Holder would have received if such Holder owned a number of Ordinary Shares equal to the Exchange Rate on the Ex-Dividend Date for such cash dividend or distribution.

(e) If Iterum or any of its Subsidiaries make a payment in respect of a tender or exchange offer for the Ordinary Shares, to the extent that the cash and value of any other consideration included in the payment per share of the Ordinary Shares exceeds the average of the Last Reported Sale Price per Ordinary Share over the 10 consecutive Trading Day period commencing on, and including, the Trading Day immediately following the last date on which tenders or exchanges may be made pursuant to such tender or exchange offer, the Exchange Rate shall be increased based on the following formula:

$$CR' = CR_0 \times \frac{AC + (SP' \times OS')}{OS_0 \times SP'}$$

where,

CR_0	=the Exchange Rate in effect immediately prior to the close of business on the 10th Trading Day immediately following, and including, the Trading Day immediately following the date such tender or exchange offer expires;
CR'	=the Exchange Rate in effect immediately after the close of business on the 10th Trading Day immediately following, and including, the Trading Day immediately following the date such tender or exchange offer expires;
AC	=the aggregate value of all cash and any other consideration (as determined by the Board of Directors in good faith) paid or payable for Ordinary Shares purchased in such tender or exchange offer;

OS_0 =the number of Ordinary Shares outstanding immediately prior to the date such tender or exchange offer expires (prior to giving effect to the purchase of all Ordinary Shares accepted for purchase or exchange in such tender or exchange offer);

OS' =the number of Ordinary Shares outstanding immediately after the date such tender or exchange offer expires (after giving effect to the purchase of all Ordinary Shares accepted for purchase or exchange in such tender or exchange offer); and

SP' =the average of the Last Reported Sale Price per Ordinary Share over the 10 consecutive Trading Day period commencing on, and including, the Trading Day immediately following the date such tender or exchange offer expires.

The increase to the Exchange Rate under this Section 14.04(e) shall occur at the close of business on the 10th Trading Day immediately following, and including, the Trading Day immediately following the date such tender or exchange offer expires; *provided* that (i) in respect of any exchange of Notes for which Physical Settlement is applicable, if the relevant Exchange Date occurs during the 10 Trading Days immediately following, and including, the Trading Day next succeeding the expiration date of any tender or exchange offer, references to "10" or "10th" in this Section 14.04(e) shall be deemed replaced with such lesser number of Trading Days as have elapsed from, and including, the Trading Day next succeeding the expiration date of such tender or exchange offer to, and including, such Exchange Date in determining the Exchange Rate and (ii) in respect of any exchange of Notes for which Cash Settlement or Combination Settlement is applicable, for any Trading Day that falls within the relevant Observation Period for such exchange and within the 10 Trading Days immediately following, and including, the Trading Day immediately following the expiration date of any tender or exchange offer, references to "10" or "10th" in this Section 14.04(e) shall be deemed replaced with such lesser number of Trading Days as have elapsed from, and including, the Trading Day next succeeding the date such tender or exchange offer expires to, and including, such Trading Day in the relevant Observation Period for purposes of determining the Exchange Rate as of such Trading Day. For the avoidance of doubt, if the application of the foregoing formula would result in a decrease in the Exchange Rate, no adjustment to the Exchange Rate will be made (other than with respect to the Company's right to readjust the Exchange Rate).

(f) *Anti-Dilution Protection* .

(i) *Adjustment of Exchange Rate Upon Issuance of Additional Ordinary Shares* . In the event Iterum shall at any time after the First Issue Date issue Additional Ordinary Shares (including Additional Ordinary Shares deemed to be issued pursuant to Section 14.04(f)(iv)), without consideration or for consideration per share less than the Exchange Price in effect immediately prior to such issuance or deemed issuance, then,

unless the Exchange Rate has been adjusted pursuant to Sections 14.04(a)-(e) above for such event, the Exchange Rate shall be increased based on the following formula:

$$CR' = CR_0 \times \frac{OS_0 + X}{OS_0 + Y}$$

where,

CR0 = the Exchange Rate in effect immediately prior to such issuance or deemed issuance of Additional Ordinary Shares;

CR' = the Exchange Rate in effect immediately after such issuance or deemed issuance of Additional Ordinary Shares;

OS0 = the number of Ordinary Shares outstanding immediately prior to such issuance or deemed issuance of Additional Ordinary Shares (treating for this purpose as outstanding all Ordinary Shares issuable upon exercise of Options outstanding immediately prior to such issuance or deemed issuance or upon conversion or exchange of Convertible Securities outstanding (assuming exercise of any outstanding Options therefor) immediately prior to such issue);

Y = the number of Ordinary Shares that would have been issued if such Additional Ordinary Shares had been issued or deemed issued at a price per share equal to the Exchange Price in effect immediately prior to such issuance or deemed issuance of Additional Ordinary Shares (determined by dividing the aggregate consideration received by Iterum in respect of such issue by such Exchange Price); and

X = the number of such Additional Ordinary Shares issued in such transaction.

The increase to the Exchange Rate under this Section 14.04(f) shall occur at the close of business on the fourth Trading Day immediately following the issuance of Additional Ordinary Shares. No adjustment in the Exchange Rate shall be made under this Section 14.04(f) as the result of the issuance or deemed issuance of Additional Ordinary Shares if Iterum receives written notice from all Holders agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Ordinary Shares.

(ii) *Determination of Consideration*. For purposes of this Section 14.04(f), the consideration received by Iterum for the issuance or deemed issuance of any Additional Ordinary Shares shall be computed as follows:

(A) *Cash and Property*: Such consideration shall:

(1) insofar as it consists of cash, be computed at the aggregate amount of cash received by Iterum, excluding amounts paid or payable for accrued interest;

(2) insofar as it consists of property other than cash, be computed at the fair market value thereof at the time of such issue, as determined in good faith by the Board of Directors of the Company; and

(3) in the event Additional Ordinary Shares are issued together with other shares or securities or other assets of Iterum for consideration which covers both, be the proportion of such consideration so received, computed as provided in clauses (1) and (2) above, as determined in good faith by the Board of Directors of the Company.

(B) *Options and Convertible Securities*. The consideration per share received by Iterum for Additional Ordinary Shares deemed to have been issued pursuant to Section 14.04(f)(iv), relating to Options and Convertible Securities, shall be determined by dividing:

(1) The total amount, if any, received or receivable by Iterum as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such consideration) payable to Iterum upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities, by

(2) the maximum number of Ordinary Shares (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities.

(iii) *Multiple Closing Dates*. In the event Iterum shall issue on more than one date Additional Ordinary Shares that are a part of one transaction or a series of related transactions and that would result in an adjustment to the Exchange Rate pursuant to the terms of Section 14.04(f)(i), and such issuance dates occur within a period of no more than ninety (90) days from the first such issuance to the final such issuance, then, upon

the election of the Board of Directors of the Company prior to the date of the first such issuance, no adjustment shall be made until the final such issuance, and upon the final such issuance, the Exchange Rate shall be adjusted to give effect to all such issuances as if they occurred on the date of the first such issuance (and without giving effect to any additional adjustments as a result of any such subsequent issuances within such period).

(iv) *Deemed Issue of Additional Ordinary Shares*.

(A) If Iterum at any time or from time to time after the First Issue Date shall issue any Options or Convertible Securities (excluding Options or Convertible Securities which are themselves Exempted Securities), then the maximum number of Ordinary Shares (as set forth in the instrument relating thereto, assuming the satisfaction of any conditions to exercisability, convertibility or exchangeability but without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Ordinary Shares issued as of the time of such issue.

(B) If the terms of any Option or Convertible Security, the issuance of which resulted in an adjustment to the Exchange Rate pursuant to the terms of Section 14.04(f)(i) are revised as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase or decrease in the number of Ordinary Shares issuable upon the exercise, conversion and/or exchange of any such Option or Convertible Security or (2) any increase or decrease in the consideration payable to Iterum upon such exercise, conversion and/or exchange, then, effective upon such increase or decrease becoming effective, the Exchange Rate computed upon the original issue of such Option or Convertible Security shall be readjusted to such Exchange Rate as would have obtained had such revised terms been in effect upon the original date of issuance of such Option or Convertible Security.

(C) If the terms of any Option or Convertible Security (excluding Options or Convertible Securities which are themselves Exempted Securities), the issuance of which did not result in an adjustment to the Exchange Rate pursuant to the terms of Section 14.04(f)(i) (either because the consideration per share (determined pursuant to Section 14.04(f)(ii)) of the Additional Ordinary Shares subject thereto was equal to or greater than the Exchange Price then in effect, or because such Option or Convertible Security was issued before the First Issue Date), are revised after the First Issue Date as a result of an amendment to

such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase in the number of Ordinary Shares issuable upon the exercise, conversion or exchange of any such Option or Convertible Security or (2) any decrease in the consideration payable to Iterum upon such exercise, conversion or exchange, then such Option or Convertible Security, as so amended or adjusted, and the Additional Ordinary Shares subject thereto (determined in the manner provided in Section 14.04(f)(iv)(A) shall be deemed to have been issued effective upon such increase or decrease becoming effective.

(D) Upon the expiration or termination of any unexercised Option or unconverted or unexchanged Convertible Security (or portion thereof) which resulted (either upon its original issuance or upon a revision of its terms) in an adjustment to the Exchange Rate pursuant to the terms of Section 14.04(f)(i), the Exchange Rate shall be readjusted to such Exchange Rate as would have obtained had such Option or Convertible Security (or portion thereof) never been issued.

(E) If the number of Ordinary Shares issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to Iterum upon such exercise, conversion and/or exchange, is calculable at the time such Option or Convertible Security is issued or amended but is subject to adjustment based upon subsequent events, any adjustment to the Exchange Rate provided for in this Section 14.04(f)(iv) shall be effected at the time of such issuance or amendment based on such number of shares or amount of consideration without regard to any provisions for subsequent adjustments (and any subsequent adjustments shall be treated as provided in clauses (B) and (C) of this Section 14.04(f)(iv)). If the number of Ordinary Shares issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to Iterum upon such exercise, conversion and/or exchange, cannot be calculated at all at the time such Option or Convertible Security is issued or amended, any adjustment to the Exchange Rate that would result under the terms of this Section 14.04(f)(iv) at the time of such issuance or amendment shall instead be effected at the time such number of shares and/or amount of consideration is first calculable (even if subject to subsequent adjustments), assuming for purposes of calculating such adjustment to the Exchange Rate that such issuance or amendment took place at the time such calculation can first be made.

(g) Notwithstanding this Section 14.04 or any other provision of this Indenture or the Notes, if an Exchange Rate adjustment becomes effective on any Ex-Dividend Date, and a Holder that has exchanged its Notes on or after such Ex-Dividend Date and on or prior to the related Record Date would be treated as the record holder of the Ordinary Shares as of the related Exchange Date as described under Section 14.02(h) based on an adjusted Exchange Rate for such Ex-Dividend Date, then, notwithstanding the Exchange Rate adjustment provisions in this Section 14.04, the Exchange Rate adjustment relating to such Ex-Dividend Date shall not be made for such exchanging Holder. Instead, such Holder shall be treated as if such Holder were the record owner of the Ordinary Shares on an unadjusted basis and participate in the related dividend, distribution or other event giving rise to such adjustment.

(h) Except as otherwise expressly stated herein, the Company shall not adjust the Exchange Rate for the issuance of Ordinary Shares or any securities convertible into or exchangeable for Ordinary Shares or the right to purchase Ordinary Shares or such convertible or exchangeable securities.

(i) In addition to those adjustments required by clauses (a), (b), (c), (d), (e) and (f) of this Section 14.04, and to the extent permitted by applicable law and subject to the applicable rules of any exchange on which any of Iterum's securities are then listed, Iterum from time to time may increase the Exchange Rate by any amount for a period of at least 20 Business Days if Iterum's Board of Directors determines that such increase would be in the Company's and/or Iterum's best interest. In addition, to the extent permitted by applicable law and subject to the applicable rules of any exchange on which any of Iterum's securities are then listed, the Company may (but is not required to) increase the Exchange Rate to avoid or diminish any income tax to holders of Ordinary Shares or rights to purchase Ordinary Shares in connection with a dividend or distribution of Ordinary Shares (or rights to acquire Ordinary Shares) or similar event. Whenever the Exchange Rate is increased pursuant to either of the preceding two sentences, the Company shall send to the Holder of each Note at its last address appearing on the Note Register a notice of the increase at least 15 days prior to the date the increased Exchange Rate takes effect, and such notice shall state the increased Exchange Rate and the period during which it will be in effect.

(j) Notwithstanding anything to the contrary in this Article 14, the Exchange Rate shall not be adjusted:

(i) upon the issuance of any Ordinary Shares pursuant to any present or future plan providing for the reinvestment of dividends or any interest payable on Iterum's securities and the investment of additional optional amounts in Ordinary Shares under any plan;

(ii) upon the issuance of any Ordinary Shares or rights, options or warrants to purchase those shares pursuant to any present or future employee, director or consultant benefit plan or program of or assumed by Iterum or any of Iterum's Subsidiaries;

(iii) upon the issuance of any Ordinary Shares pursuant to any right, option, warrant or exercisable, exchangeable or convertible security not described in clause (ii) of this subsection and outstanding as of the date the Notes were first issued;

(iv) upon the repurchase of Ordinary Shares pursuant to an open-market share repurchase program or other buy-back transaction that is not a tender offer or exchange offer of the nature described in Section 14.04(e);

(v) solely for a change in the par value of the Ordinary Shares; or

(vi) for accrued and unpaid interest, if any, on the Notes.

(k) The Company shall not be required to make an adjustment pursuant to clauses (a), (b), (c), (d), (e) or (f) of this Section 14.04 unless such adjustment would result in a change of at least 1% of the then effective Exchange Rate. However, the Company shall carry forward any adjustment that the Company would otherwise have to make and take that adjustment into account in any subsequent adjustment. Notwithstanding the foregoing, all such carried-forward adjustments shall be made with respect to the Notes (i) in connection with any subsequent adjustment to the Exchange Rate of at least 1% of the Exchange Rate (when such carried-forward adjustments are taken into account) and (ii) (x) on the Exchange Date for any Notes (in the case of Physical Settlement) and (y) on each Trading Day of any Observation Period (in the case of Cash Settlement or Combination Settlement). All calculations and other determinations under this Article 14 shall be made by the Company and shall be made to the nearest one-ten thousandth (1/10,000) of a share.

(l) Whenever the Exchange Rate is adjusted as herein provided, the Company shall promptly file with the Trustee (and the Exchange Agent if not the Trustee) an Officer's Certificate setting forth the Exchange Rate after such adjustment and setting forth a brief statement of the facts requiring such adjustment. Unless and until a Responsible Officer of the Trustee shall have received such Officer's Certificate, the Trustee shall not be deemed to have knowledge of any adjustment of the Exchange Rate and may assume without inquiry that the last Exchange Rate of which it has knowledge is still in effect. Promptly after delivery of such certificate, the Company shall prepare a notice of such adjustment of the Exchange Rate setting forth the adjusted Exchange Rate and the date on which each adjustment becomes effective and shall send such notice of such adjustment of the Exchange Rate to each Holder at its last address appearing on the Note Register of this Indenture. Failure to deliver such notice shall not affect the legality or validity of any such adjustment.

(m) For purposes of this Section 14.04, the number of Ordinary Shares at any time outstanding shall not include Ordinary Shares held in the treasury of Iterum so long as Iterum does not pay any dividend or make any distribution on Ordinary Shares held in the treasury of Iterum, but shall include Ordinary Shares issuable in respect of scrip certificates issued in lieu of fractions of Ordinary Shares.

Section 14.05 *Adjustments of Prices.* Whenever any provision of this Indenture requires the Company to calculate the Last Reported Sale Prices, the Daily VWAPs, the Daily Exchange Values or the Daily Settlement Amounts over a span of multiple days (including without limitation, an Observation Period), the Company shall make appropriate adjustments to each to account for any adjustment to the Exchange Rate that becomes effective, or any event requiring an adjustment to the Exchange Rate where the Ex-Dividend Date of the event occurs, at any time during the period when the Last Reported Sale Prices, the Daily VWAPs, the Daily Exchange Values or the Daily Settlement Amounts are to be calculated.

Section 14.06 *Shares to Be Fully Paid.* Subject to the valid passing of the Authorized Shares Approval by the requisite majority of shareholders at a duly convened shareholder meeting, Iterum shall, and the Company shall cause Iterum to, reserve, free from preemptive rights, out of Iterum's authorized but unissued shares or shares held in treasury, sufficient Ordinary Shares to provide for exchange of the Notes from time to time as such Notes are presented for exchange (assuming that at the time of computation of such number of shares, all such Notes would be exchanged by a single Holder and that Physical Settlement is applicable).

Section 14.07 *Effect of Recapitalizations, Reclassifications and Changes of the Ordinary Shares.*

(a) In the case of:

(i) any recapitalization, reclassification or change of the Ordinary Shares (other than changes resulting from a subdivision or combination),

(ii) any consolidation, merger or combination involving Iterum,

(iii) any sale, lease or other transfer to a third party of the consolidated assets of Iterum and its Subsidiaries substantially as an entirety or

(iv) any statutory share exchange,

in each case, as a result of which the Ordinary Shares would be converted into, or exchanged for, stock, other securities, other property or assets (including cash or any combination thereof) (any such event, a "**Specified Transaction** "), then, subject to Section 15.02 to the extent such Specified Transaction is a Fundamental Change, at and after the effective time of such Specified Transaction, the right to exchange each $1,000 of principal of and accrued but unpaid interest on

the Notes being exchanged shall be changed into a right to exchange such principal amount of Notes into the kind and amount of shares of stock, other securities or other property or assets (including cash or any combination thereof) that a holder of a number of Ordinary Shares equal to the Exchange Rate immediately prior to such Specified Transaction would have owned or been entitled to receive (the "**Reference Property**", with each "**unit of Reference Property**" meaning the kind and amount of Reference Property that a holder of one Ordinary Share is entitled to receive) upon such Specified Transaction and, prior to or at the effective time of such Specified Transaction, the Company and the Guarantors and/or the successor or purchasing Person, as the case may be, shall execute with the Trustee a supplemental indenture permitted under Section 10.01(n) providing for such change in the right to exchange each $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged; *provided*, *however*, that at and after the effective time of the Specified Transaction (A) the Company or the successor or purchasing Person, as the case may be, shall continue to have the right to determine the form of consideration to be paid or delivered, as the case may be, upon exchange of Notes in accordance with Section 14.02 and (B) (I) any amount payable in cash upon exchange of the Notes in accordance with Section 14.02 shall continue to be payable in cash, (II) any Ordinary Shares that the Company would have been required to deliver upon exchange of the Notes in accordance with Section 14.02 shall instead be deliverable in the amount and type of Reference Property that a holder of that number of Ordinary Shares would have received in such Specified Transaction and (III) the Daily VWAP shall be calculated based on the value of a unit of Reference Property.

If the Specified Transaction causes the Ordinary Shares to be converted into, or exchanged for, the right to receive more than a single type of consideration (determined based in part upon any form of shareholder election), then (i) the Reference Property into which the Notes will be exchangeable shall be deemed to be the weighted average of the types and amounts of consideration actually received by the holders of Ordinary Shares, and (ii) the unit of Reference Property for purposes of the immediately preceding paragraph shall refer to the consideration referred to in clause (i) attributable to one Ordinary Share. If the holders of Ordinary Shares receive only cash in such Specified Transaction, then for all exchanges that occur after the effective date of such Specified Transaction (A) the consideration due upon exchange of each $1,000 of principal of and accrued but unpaid interest on the Notes being exchanged shall be solely cash in an amount equal to the Exchange Rate in effect on the Exchange Date, *multiplied by* the price paid per Ordinary Share in such Specified Transaction and (B) the Company shall satisfy the Exchange Obligation by paying cash to exchanging Holders on the second Business Day immediately following the relevant Exchange Date. The Company shall notify Holders, the Trustee and the Exchange Agent (if other than the Trustee) of such weighted average as soon as practicable after such determination is made.

Such supplemental indenture described in the second immediately preceding paragraph shall provide for adjustments that shall be as nearly equivalent as is possible to the adjustments provided for in this Article 14. If, in the case of any Specified Transaction, the Reference

Property includes shares of stock, securities or other property or assets (including cash or any combination thereof) of a Person other than the Company, the Guarantors and/or the successor or purchasing corporation, as the case may be, in such Specified Transaction, then such supplemental indenture shall also be executed by such other Person and shall contain such additional provisions to protect the interests of the Holders of the Notes as the Board of Directors shall reasonably consider necessary by reason of the foregoing, including the provisions providing for the purchase rights set forth in Article 15.

(b) When the Company or the Guarantors execute a supplemental indenture pursuant to subsection (a) of this Section 14.07, the Company shall promptly file with the Trustee an Officer's Certificate briefly stating the reasons therefor, the kind or amount of cash, securities or property or asset that will comprise a unit of Reference Property after any such Specified Transaction, any adjustment to be made with respect thereto and that all conditions precedent have been complied with and an Opinion of Counsel stating that all conditions precedent have been complied with, and shall promptly send notice thereof to all Holders. The Company shall cause notice of the execution of such supplemental indenture to be sent to each Holder, at its address appearing on the Note Register provided for in this Indenture, within 20 days after execution thereof. Failure to deliver such notice shall not affect the legality or validity of such supplemental indenture.

(c) Neither the Company nor the Guarantors shall become a party to any Specified Transaction unless its terms are consistent with this Section 14.07. None of the foregoing provisions shall affect the right of a holder of Notes to exchange its Notes into cash, Ordinary Shares or a combination of cash and Ordinary Shares, as applicable, as set forth in Section 14.01 and Section 14.02 prior to the effective date of such Specified Transaction.

(d) The above provisions of this Section shall similarly apply to successive Specified Transactions.

(e) Upon the consummation of any Specified Transaction, references to "Ordinary Shares" shall be deemed to refer to any Reference Property that constitutes Common Equity after giving effect to such Specified Transaction.

Section 14.08 *Certain Covenants.* (a) Each of the Company and Iterum covenants that all Ordinary Shares issued upon exchange of Notes will be newly issued shares or treasury shares, duly authorized, fully paid and not subject to any calls for any additional payments (non-assessable) and free from all taxes, liens and charges with respect to the issuance thereof.

(b) Iterum covenants that, if any Ordinary Shares to be provided for the purpose of exchange of Notes hereunder require registration with or approval of any governmental authority under any federal or state law before such Ordinary Shares may be validly issued upon exchange, Iterum will, to the extent then permitted by the rules and interpretations of the Commission, secure such registration or approval, as the case may be.

(c) Iterum further covenants that if at any time the Ordinary Shares shall be listed on any national securities exchange or automated quotation system Iterum will list and keep listed, so long as the Ordinary Shares shall be so listed on such exchange or automated quotation system, any Ordinary Shares issuable upon exchange of the Notes.

Section 14.09 *Responsibility of Trustee.* The Trustee and any other Exchange Agent shall not at any time be under any duty or responsibility to any Holder to determine the Exchange Rate (or any adjustment thereto) or whether any facts exist that may require any adjustment (including any increase) of the Exchange Rate, or with respect to the nature or extent or calculation of any such adjustment when made, or with respect to the method employed, or herein or in any supplemental indenture provided to be employed, in making the same. The Trustee and any other Exchange Agent shall not be accountable with respect to the validity or value (or the kind or amount) of any Ordinary Shares, or of any securities, property or cash that may at any time be issued or delivered upon the exchange of any Note; and the Trustee and any other Exchange Agent make no representations with respect thereto. Neither the Trustee nor any Exchange Agent shall be responsible for any failure of the Company to issue, transfer or deliver any Ordinary Shares or stock certificates or other securities or property or cash upon the surrender of any Note for the purpose of exchange or to comply with any of the duties, responsibilities or covenants of the Company contained in this Article. Without limiting the generality of the foregoing, neither the Trustee nor any Exchange Agent shall be under any responsibility to determine the correctness of any provisions contained in any supplemental indenture entered into pursuant to Section 14.07 relating either to the kind or amount of shares of stock or securities or property (including cash) receivable by Holders upon the exchange of their Notes after any event referred to in such Section 14.07 or to any adjustment to be made with respect thereto, but, subject to the provisions of Section 7.01, may accept (without any independent investigation) as conclusive evidence of the correctness of any such provisions, and shall be protected in conclusively relying upon, the Officer's Certificate and Opinion of Counsel (which the Company shall be obligated to file with the Trustee prior to the execution of any such supplemental indenture) with respect thereto. Neither the Trustee nor the Exchange Agent shall be responsible for determining whether any event contemplated by Section 14.01 has occurred that makes the Notes eligible for exchange or no longer eligible therefor until the Company has delivered to the Trustee and the Exchange Agent the notices referred to in Section 14.01 with respect to the commencement or termination of such exchange rights, on which notices the Trustee and the Exchange Agent may conclusively rely, and the Company agrees to deliver such notices to the Trustee and the Exchange Agent immediately after the occurrence of any such event or at such other times as shall be provided for in Section 14.01. The parties agree that all notices to the Trustee or the Exchange Agent under this Article 14 must be in writing.

Section 14.10 *Notice to Holders Prior to Certain Actions.* In case of any:

(a) action by the Company, Iterum or one of their Subsidiaries that would require an adjustment in the Exchange Rate pursuant to Section 14.04 or Section 14.11 (other than Section 14.04(f));

(b) Specified Transaction; or

(c) voluntary or involuntary dissolution, liquidation or winding-up of the Company, the Guarantors or any of their respective Subsidiaries;

then, in each case (unless notice of such event is otherwise required pursuant to another provision of this Indenture), the Company shall cause to be filed with the Trustee and the Exchange Agent (if other than the Trustee) and to be sent to each Holder at its address appearing on the Note Register, as promptly as possible but in any event at least 20 days prior to the applicable date hereinafter specified, a notice stating (i) the date on which a record is to be taken for the purpose of such action by the Company, the Guarantors or one of their Subsidiaries or, if a record is not to be taken, the date as of which the holders of Ordinary Shares of record are to be determined for the purposes of such action by the Company, the Guarantors or one of their Subsidiaries, or (ii) the date on which such Specified Transaction, dissolution, liquidation or winding-up is expected to become effective or occur, and the date as of which it is expected that holders of Ordinary Shares of record shall be entitled to exchange their Ordinary Shares for securities or other property deliverable upon such Specified Transaction, dissolution, liquidation or winding-up.

In case of any action by Iterum that would require an adjustment in the Exchange Rate pursuant to Section 14.04(f), then (unless notice of such event is otherwise required pursuant to another provision of this Indenture), the Company shall cause to be filed with the Trustee and the Exchange Agent (if other than the Trustee) and to be mailed to each Holder at its address appearing on the Note Register, as promptly as possible but in any event at least 10 days following the date on which the Additional Ordinary Shares were issued (or deemed to be issued), a notice stating the date on which such issuance occurred.

Failure to give any of the forgoing notices, or any defect therein, shall not affect the legality or validity of such action by the Company, the Guarantors or one of their Subsidiaries, Specified Transaction, dissolution, liquidation, winding-up or issuance of Additional Ordinary Shares.

Section 14.11 *Shareholder Rights Plans.* If Iterum has a shareholder rights plan in effect upon exchange of the Notes, each Ordinary Shares, if any, delivered upon such exchange shall be entitled to receive the appropriate number of rights, if any, and the certificates representing the Ordinary Shares issued upon such exchange shall bear such legends, if any, in each case as may be provided by the terms of any such shareholder rights plan, as the same may be amended from time to time. However, if, prior to any exchange of Notes, the rights have separated from the Ordinary Shares in accordance with the provisions of the applicable shareholder rights plan so

that the Holders would not be entitled to receive any rights in respect of Ordinary Shares, if any, issuable upon exchange of the Notes, the Exchange Rate shall be adjusted at the time of separation as if Iterum distributed to all or substantially all holders of the Ordinary Shares Distributed Property as provided in Section 14.04(c), subject to readjustment in the event of the expiration, termination or redemption of such rights.

ARTICLE 15
Repurchase of Notes

Section 15.01 *Intentionally Omitted.*

Section 15.02 *Repurchase at Option of Holders Upon a Fundamental Change.* (a) If a Fundamental Change occurs at any time prior to the Interest Record Date, each Holder shall have the right, at such Holder's option, to require the Company to repurchase for cash all of such Holder's Notes, or any portion thereof that is equal to a minimum of $1,000 principal amount or a multiple of $1,000 in excess thereof, on the date (the "**Fundamental Change Repurchase Date**") specified by the Company that is not less than 20 calendar days or more than 35 calendar days following the date of the Fundamental Change Company Notice at a repurchase price equal to (i) with respect to a Fundamental Change that is not a Liquidation Event, the Change of Control Price or (ii) with respect to a Fundamental Change that is a Liquidation Event, 100% of the principal amount thereof, *plus*, in each case, any accrued and unpaid interest thereon to, but excluding, the Fundamental Change Repurchase Date (the "**Fundamental Change Repurchase Price**").

(b) Repurchases of Notes under this Section 15.02 shall be made, at the option of the Holder thereof, upon:

(i) delivery to the Paying Agent by a Holder of a duly completed notice (the "**Fundamental Change Repurchase Notice**") in the form set forth in Attachment 2 to the Form of Note attached hereto as Exhibit A, if the Notes are Physical Notes, or in compliance with the Depositary's procedures for surrendering interests in Global Notes, if the Notes are Global Notes, in each case on or before the close of business on the Business Day immediately preceding the Fundamental Change Repurchase Date; and

(ii) delivery of the Notes, if the Notes are Physical Notes, to the Paying Agent at any time after delivery of the Fundamental Change Repurchase Notice (together with all necessary endorsements for transfer) at the Corporate Trust Office of the Paying Agent, or book-entry transfer of the Notes, if the Notes are Global Notes, in compliance with the procedures of the Depositary, in each case such delivery being a condition to receipt by the Holder of the Fundamental Change Repurchase Price therefor.

The Fundamental Change Repurchase Notice in respect of any Notes to be repurchased shall state:

(i) in the case of Physical Notes, the certificate numbers of the Notes to be delivered for repurchase;

(ii) the portion of the principal amount of Notes to be repurchased, which must be a minimum of $1,000 or a multiple of $1,000 in excess thereof; and

(iii) that the Notes are to be repurchased by the Company pursuant to the applicable provisions of the Notes and this Indenture;

provided, *however*, that if the Notes are Global Notes, the Fundamental Change Repurchase Notice must comply with appropriate Depositary procedures.

Notwithstanding anything herein to the contrary, any Holder delivering to the Paying Agent the Fundamental Change Repurchase Notice contemplated by this Section 15.02 shall have the right to withdraw, in whole or in part, such Fundamental Change Repurchase Notice at any time prior to the close of business on the Business Day immediately preceding the Fundamental Change Repurchase Date by delivery of a written notice of withdrawal to the Paying Agent in accordance with Section 15.03.

The Paying Agent shall promptly notify the Company of the receipt by it of any Fundamental Change Repurchase Notice or written notice of withdrawal thereof.

(c) On or before the 10th Business Day after the effective date of a Fundamental Change, the Company shall provide to all Holders of Notes and the Trustee, the Exchange Agent (in the case of an Exchange Agent other than the Trustee) and the Paying Agent (in the case of a Paying Agent other than the Trustee) a notice (the "**Fundamental Change Company Notice**") of the effective date of the Fundamental Change and of the repurchase right at the option of the Holders arising as a result thereof. In the case of Physical Notes, such notice shall be by first class mail or, in the case of Global Notes, such notice shall be delivered in accordance with the applicable procedures of the Depositary. Each Fundamental Change Company Notice shall specify:

(i) the events causing the Fundamental Change;

(ii) the effective date of the Fundamental Change;

(iii) the last date on which a Holder may exercise the repurchase right pursuant to this Article 15;

(iv) the Fundamental Change Repurchase Price;

(v) the Fundamental Change Repurchase Date;

(vi) the name and address of the Paying Agent and the Exchange Agent, if applicable;

(vii) that the Notes are eligible to be exchanged and, if applicable, the Exchange Rate and any adjustments to the Exchange Rate;

(viii) that the Notes with respect to which a Fundamental Change Repurchase Notice has been delivered by a Holder may be exchanged only if the Holder withdraws the Fundamental Change Repurchase Notice in accordance with the terms of this Indenture; and

(ix) the procedures that Holders must follow to require the Company to repurchase their Notes.

No failure of the Company to give the foregoing notices and no defect therein shall limit the Holders' repurchase rights or affect the validity of the proceedings for the repurchase of the Notes pursuant to this Section 15.02.

At the Company's request, the Trustee shall give such notice in the Company's name and at the Company's expense; *provided*, *however*, that, in all cases, the text of such Fundamental Change Company Notice shall be prepared by the Company and such request shall be made by the Company at least five Business Days (or such shorter period as may be agreed to by the Trustee) prior to the date such notice is required to be sent to Holders.

(d) Notwithstanding the foregoing, no Notes may be repurchased by the Company on any date at the option of the Holders upon a Fundamental Change if the principal amount of the Notes has been accelerated, and such acceleration has not been rescinded, on or prior to such date (except in the case of an acceleration resulting from a Default by the Company in the payment of the Fundamental Change Repurchase Price with respect to such Notes). The Paying Agent will promptly return to the respective Holders thereof any Physical Notes held by it during the acceleration of the Notes (except in the case of an acceleration resulting from a Default by the Company in the payment of the Fundamental Change Repurchase Price with respect to such Notes), or any instructions for book-entry transfer of the Notes in compliance with the procedures of the Depositary shall be deemed to have been cancelled, and, upon such return or cancellation, as the case may be, the Fundamental Change Repurchase Notice with respect thereto shall be deemed to have been withdrawn.

Section 15.03 *Withdrawal of Fundamental Change Repurchase Notice.* (a) A Fundamental Change Repurchase Notice may be withdrawn (in whole or in part) by means of a written notice of withdrawal delivered to the Paying Agent in accordance with this Section 15.03 at any time prior to the close of business on the Business Day immediately preceding the Fundamental Change Repurchase Date, specifying:

(i) the principal amount of the Notes with respect to which such notice of withdrawal is being submitted,

(ii) if Physical Notes have been issued, the certificate number of the Note in respect of which such notice of withdrawal is being submitted, and

(iii) the principal amount, if any, of such Note that remains subject to the original Fundamental Change Repurchase Notice, which portion must be in a minimum principal amount of $1,000 or a multiple of $1,000 in excess thereof;

provided, *however*, that if the Notes are Global Notes, the notice must comply with appropriate procedures of the Depositary.

Section 15.04 *Deposit of Fundamental Change Repurchase Price.* (a) The Company will deposit with the Trustee (or other Paying Agent appointed by the Company, or if the Company is acting as its own Paying Agent, set aside, segregate and hold in trust as provided in Section 4.04) on or prior to 11:00 a.m., New York City time, on the Fundamental Change Repurchase Date an amount of money sufficient to repurchase all of the Notes to be repurchased at the appropriate Fundamental Change Repurchase Price; provided, that to the extent such deposit is received by the Paying Agent after 11:00 a.m. New York City time, on any such due date, such deposit will be deemed deposited on the next Business Day. Subject to receipt of funds and/or Notes by the Trustee (or other Paying Agent appointed by the Company), payment for Notes surrendered for repurchase (and not withdrawn prior to the close of business on the Business Day immediately preceding the Fundamental Change Repurchase Date) will be made on the later of (i) the Fundamental Change Repurchase Date (*provided* the Holder has satisfied the conditions in Section 15.02) and (ii) the time of book-entry transfer or the delivery of such Note to the Trustee (or other Paying Agent appointed by the Company) by the Holder thereof in the manner required by Section 15.02 by sending checks for the amount payable to the Holders of such Notes entitled thereto as they shall appear in the Note Register; *provided*, *however*, that payments to the Depositary shall be made by wire transfer of immediately available funds to the account of the Depositary or its nominee. The Trustee or Paying Agent shall, promptly after such payment and upon written demand by the Company, return to the Company any funds in excess of the Fundamental Change Repurchase Price.

(b) If by 11:00 a.m. New York City time, on the Fundamental Change Repurchase Date, the Trustee (or other Paying Agent appointed by the Company) holds money sufficient to make payment on all the Notes or portions thereof that are to be repurchased on such Fundamental Change Repurchase Date, then, with respect to the Notes that have been properly surrendered for repurchase and have not been validly withdrawn in accordance with the provisions of this Indenture, (i) such Notes will cease to be outstanding, (ii) interest will cease to accrue on such Notes (whether or not book-entry transfer of the Notes has been made or the Notes have been delivered to the Trustee or Paying Agent) and (iii) all other rights of the Holders

of such Notes will terminate (other than the right to receive the Fundamental Change Repurchase Price).

(c) Upon surrender of a Note that is to be repurchased in part pursuant to Section 15.02, the Company shall execute and the Trustee shall authenticate and deliver to the Holder a new Note in an authorized denomination equal in principal amount to the unrepurchased portion of the Note surrendered.

Section 15.05 *Covenant to Comply with Applicable Laws Upon Repurchase of Notes.* In connection with any repurchase offer, the Company will, if required:

(a) comply with the provisions of Rule 13e-4, Rule 14e-1 and any other tender offer rules under the Exchange Act;

(b) file a Schedule TO or any other required schedule under the Exchange Act; and

(c) otherwise comply with all federal and state securities laws in connection with any offer by the Company to repurchase the Notes;

in each case, so as to permit the rights and obligations under this Article 15 to be exercised in the time and in the manner specified in this Article 15.

ARTICLE 16
Optional Redemption

Section 16.01 *Optional Redemption*. No sinking fund is provided for the Notes. The Company may at any time on or after the earliest of (i) the later of (x) the date on which the Individual Ownership Cap, the Aggregate Ownership Cap and the Available Shares Ownership Cap no longer apply and (y) January 21, 2021, (ii) the consummation of a Fundamental Change and (iii) the date that Iterum enters into a definitive agreement relating to a Fundamental Change that has been approved by the Board of Directors of Iterum, and in each case upon receipt of written consent of the holders of the Senior Debt while the Senior Debt remains outstanding, redeem (an "**Optional Redemption**") for cash all or any portion of the Notes, at the Redemption Price.

Section 16.02 *Notice of Optional Redemption; Selection of Notes*. (a) In case the Company exercises its Optional Redemption right to redeem all or, as the case may be, any part of the Notes pursuant to Section 16.01, it shall fix a date for redemption (each, a "**Redemption Date**") and it or, at its written request received by the Trustee not less than 75 Scheduled Trading Days prior to the Redemption Date (or such shorter period of time as may be acceptable to the Trustee), the Trustee, in the name of and at the expense of the Company, shall deliver or cause to be delivered a notice of such Optional Redemption (a "**Redemption Notice**") not less than 60 nor more than 70 Scheduled Trading Days prior to the Redemption Date to each Holder of Notes

so to be redeemed as a whole or in part;*provided*, *however*, that, if the Company shall give such notice, it shall also give written notice of the Redemption Date to the Trustee and the Paying Agent (if other than the Trustee). However, if in accordance with Section 14.02(a)(ii), the Company elects to settle all exchanges with an Exchange Date that occurs on or after the date of the Redemption Notice and before the related Redemption Date by Physical Settlement, then the Company may instead provide such Redemption Notice not less than 30 nor more than 45 calendar days prior to the Redemption Date. A Redemption Notice may, at the discretion of the Company, be subject to one or more conditions precedent, including, but not limited to, completion of an equity offering, a financing, or other corporate transaction. If a Redemption Notice is subject to any conditions precedent, the Company shall provide the Trustee with written notice of such conditions precedent. The Redemption Date must be a Business Day.

(b) The Redemption Notice, if delivered in the manner herein provided, shall be conclusively presumed to have been duly given, whether or not the Holder receives such notice. In any case, failure to give such Redemption Notice or any defect in the Redemption Notice to the Holder of any Note designated for redemption as a whole or in part shall not affect the validity of the proceedings for the redemption of any other Note.

(c) Each Redemption Notice shall specify:

(i) the Redemption Date;

(ii) the Redemption Price;

(iii) that on the Redemption Date, the Redemption Price will become due and payable upon each Note to be redeemed, and that interest thereon, if any, shall cease to accrue on and after the Redemption Date;

(iv) the place or places where such Notes are to be surrendered for payment of the Redemption Price;

(v) that Holders may surrender their Notes for exchange at any time prior to the close of business on the Scheduled Trading Day immediately preceding the Redemption Date;

(vi) the procedures an exchanging Holder must follow to exchange its Notes and the Settlement Method and Specified Dollar Amount, if applicable;

(vii) the Exchange Rate;

(viii) the CUSIP, ISIN or other similar numbers, if any, assigned to such Notes;

(ix) in case any Note is to be redeemed in part only, the portion of the principal amount thereof to be redeemed and on and after the Redemption Date, upon surrender of such Note, a new Note in principal amount equal to the unredeemed portion thereof shall be issued; and

(x) if such Redemption Notice is subject to one or more conditions precedent, then, in the Company's discretion, the Redemption Date may be postponed until up to 80 days (or, if in accordance with Section 14.02(a)(ii), the Company elects to settle all exchanges with an Exchange Date that occurs on or after the date of the Redemption Notice and before the related Redemption Date by Physical Settlement, then 50 days) following the Redemption Notice, and that such notice may be rescinded in the event that any or all such conditions shall not have been satisfied by the Redemption Date (including as it may be postponed).

Unless a Redemption Notice is subject to one or more conditions precedent as set forth in the second to last sentence of Section 16.02(a), a Redemption Notice shall be irrevocable.

(d) If fewer than all of the outstanding Notes are to be redeemed, the Trustee shall select the Notes or portions thereof of a Global Note or the Notes in certificated form to be redeemed (in principal amounts of $1,000 or multiples thereof) by lot, on a *pro rata* basis or by another method the Trustee considers to be fair and appropriate or as required by the rules and procedures of the Depository. If any Note selected for partial redemption is submitted for exchange in part after such selection, the portion of the Note submitted for exchange shall be deemed (so far as may be possible) to be the portion selected for redemption.

Section 16.03 *Payment of Notes Called for Redemption.* (a) If any Redemption Notice has been given in respect of the Notes in accordance with Section 16.02, the Notes shall become due and payable on the Redemption Date at the place or places stated in the Redemption Notice and at the applicable Redemption Price. On presentation and surrender of the Notes at the place or places stated in the Redemption Notice, the Notes shall be paid and redeemed by the Company at the applicable Redemption Price.

(b) Prior to the open of business on the Redemption Date, the Company shall deposit with the Paying Agent or, if the Guarantors, the Company or a respective Subsidiary of a Guarantor or the Company is acting as the Paying Agent, shall segregate and hold in trust as provided in Section 7.05 an amount of cash (in immediately available funds if deposited on the Redemption Date), sufficient to pay the Redemption Price of all of the Notes to be redeemed on such Redemption Date. Subject to receipt of funds by the Paying Agent, payment for the Notes to be redeemed shall be made on the Redemption Date for such Notes. The Paying Agent shall, promptly after such payment and upon written demand by the Company, return to the Company any funds in excess of the Redemption Price.

(c) If any Change of Control Transaction is consummated within 120 days of any Redemption Date, and the Company failed to pay a Redemption Price on such Redemption Date equal to the Change of Control Price, plus any accrued and unpaid interest in accordance with the definition of Redemption Price, then concurrently with the consummation of such transaction the Company shall pay to the former Holders of such Notes an amount representing the shortfall between the Change of Control Price, plus any accrued and unpaid interest as described in the definition of Redemption Price, and the amount actually paid by the Company on such Redemption Date.

Section 16.04 *Restrictions on Redemption.* The Company may not redeem any Notes if the Redemption Date would fall after the Maturity Date. In addition, no Notes may be redeemed on any date if the principal amount of the Notes has been accelerated in accordance with the terms of this Indenture, and such acceleration has not been rescinded, on or prior to the Redemption Date (except in the case of an acceleration resulting from a Default by the Company in the payment of the Redemption Price with respect to such Notes).

ARTICLE 17
Miscellaneous Provisions

Section 17.01 *Provisions Binding on Successors.* All the covenants, stipulations, promises and agreements of each of the Company and the Guarantors contained in this Indenture shall bind its successors and assigns whether so expressed or not.

Section 17.02 *Official Acts by Successor Corporation.* Any act or proceeding by any provision of this Indenture authorized or required to be done or performed by any board, committee or Officer of the Company or any Guarantor shall and may be done and performed with like force and effect by the like board, committee or officer of any corporation or other entity that shall at the time be the lawful sole successor of the Company or such Guarantor, as the case may be.

Section 17.03 *Addresses for Notices, Etc.* Any notice or demand that by any provision of this Indenture is required or permitted to be given or made by the Trustee or by the Holders on the Company or the Guarantors shall be deemed to have been sufficiently given or made, for all purposes if given or made by being deposited postage prepaid by registered or certified mail in a post office letter box addressed (until another address is filed by the Company or the Guarantors with the Trustee) to Iterum Therapeutics plc, Block 2, Floor 3 Harcourt Centre, Harcourt Street, Dublin 2, Ireland, Attention: Corey Fishman, with a copy to Iterum Therapeutics plc, Legal Department, Block 2, Floor 3 Harcourt Centre, Harcourt Street, Dublin 2, Ireland. Any notice, direction, request or demand hereunder to or upon the Trustee shall be in writing (including facsimile or electronic transmission in PDF format). Notices by certified or registered mail shall be deemed to have been sufficiently given or made, for all purposes, if given or made by being deposited postage prepaid by registered or certified mail in a post office letter box addressed to

the Corporate Trust Office or sent electronically in PDF format and, in each case, upon actual receipt by the Trustee. Notice to the Trustee by electronic shall be deemed to have been sufficiently given or made, for all purposes, if sent to cts.conversions@usbank.com or such other email address as the Trustee may from time to time designate in writing to the Company the Holders absent receipt of a failure to deliver notice.

The Trustee agrees to accept and act upon instructions or directions pursuant to this Indenture sent by unsecured e-mail, pdf, facsimile transmission or other similar unsecured electronic methods, *provided* that the Trustee shall have received an incumbency certificate listing persons designated to give such instructions or directions and containing specimen signatures of such designated persons, which such incumbency certificate shall be amended and replaced whenever a person is to be added or deleted from the listing.

The Trustee, by notice to the Company, may designate additional or different addresses for subsequent notices or communications.

Any notice or communication sent to a Holder of Physical Notes shall be mailed to it by first class mail, postage prepaid, at its address as it appears on the Note Register and shall be sufficiently given to it if so mailed within the time prescribed. Any notice or communication sent to Holders of Global Notes shall be sent in accordance with the applicable procedures of the Depositary and shall be sufficiently given to it if so sent within the time prescribed.

Failure to deliver a notice or communication to a Holder or any defect in it shall not affect its sufficiency with respect to other Holders. If a notice or communication is sent or delivered in the manner provided above, it is duly given, whether or not the addressee receives it.

In case by reason of the suspension of regular mail service or by reason of any other cause it shall be impracticable to give such notice to Holders by mail, then such notification as shall be made with the approval of the Trustee shall constitute a sufficient notification for every purpose hereunder.

In addition to the foregoing, the Trustee agrees to accept and act upon notice, instructions or directions pursuant to this Indenture sent by unsecured e-mail, facsimile transmission or other similar unsecured electronic methods. If the party elects to give the Trustee e-mail or facsimile instructions (or instructions by a similar electronic method), and the Trustee acts upon such instructions, the Trustee's understanding of such instructions shall be deemed controlling. The Trustee shall not be liable for any losses, costs or expenses arising directly or indirectly from the Trustee's reliance upon and compliance with such instructions notwithstanding such instructions conflict or are inconsistent with a subsequent written instruction. The party providing electronic instructions agrees to assume all risks arising out of the use of such electronic methods to submit instructions and directions to the Trustee, including, without limitation, the risk of the Trustee acting on unauthorized instructions, and the risk or interception and misuse by third parties.

Section 17.04 *Governing Law; Jurisdiction.* THIS INDENTURE, THE GUARANTEE AND EACH NOTE, AND ANY CLAIM, CONTROVERSY OR DISPUTE ARISING UNDER OR RELATED TO THIS INDENTURE, THE GUARANTEE AND EACH NOTE, SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH, THE LAWS OF THE STATE OF NEW YORK.

Each of the Company and the Guarantors irrevocably consents and agrees, for the benefit of the Holders from time to time of the Notes and the Trustee, that any legal action, suit or proceeding against it with respect to obligations, liabilities or any other matter arising out of or in connection with this Indenture, the Guarantee or the Notes may be brought in the courts of the State of New York or the courts of the United States located in the Borough of Manhattan, New York City, New York and, until amounts due and to become due in respect of the Notes have been paid, hereby irrevocably consents and submits to the non-exclusive jurisdiction of each such court *in personam*, generally and unconditionally with respect to any action, suit or proceeding for itself in respect of its properties, assets and revenues.

Each of the Company and the Guarantors irrevocably and unconditionally waives, to the fullest extent permitted by law, any objection which it may now or hereafter have to the laying of venue of any of the aforesaid actions, suits or proceedings arising out of or in connection with this Indenture, the Notes or the Guarantee brought in the courts of the State of New York or the courts of the United States located in the Borough of Manhattan, New York City, New York and hereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum.

Section 17.05 *Evidence of Compliance with Conditions Precedent; Certificates and Opinions of Counsel to Trustee.* Upon any application or demand by the Company or any Guarantor to the Trustee to take any action under any of the provisions of this Indenture, the Company or such Guarantors, as applicable, shall furnish to the Trustee an Officer's Certificate and/or Opinion of Counsel, subject to customary exceptions, in form and substance reasonably satisfactory to the Trustee, stating that such action is permitted by the terms of the Indenture and that all conditions precedent, if any, provided for in this Indenture relating to the proposed action have been complied with, except that, in the case of any such application or request as to which the furnishing of such documents is specifically required by any provision of this Indenture relating to such particular application or request, no additional certificate or opinion need be furnished.

Each Officer's Certificate or Opinion of Counsel provided for in this Indenture and delivered to the Trustee with respect to compliance with a condition or covenant provided for in this Indenture shall include (a) a statement that the person signing such Officer's Certificate or Opinion of Counsel has read such covenant or condition, (b) a brief statement as to the nature and scope of the examination or investigation upon which the statements or opinions contained

in such Officer's Certificate or Opinion of Counsel are based, (c) a statement that, in the opinion of such person, he or she has made such examination or investigation as is necessary to enable him or her to express an informed opinion as to whether or not such action is permitted by this Indenture and whether or not such covenants or conditions have been complied with and (d) a statement as to whether or not, in the opinion of such person, such action is permitted by this Indenture and that all conditions or covenants precedent to such action have been complied with.

Any Officer's Certificate of the Company or any Guarantor may be based, insofar as it relates to legal matters, upon an Opinion of Counsel, unless such officer knows that the Opinion of Counsel with respect to the matters upon which his or her Officer's Certificate may be based as aforesaid are erroneous, or in the exercise of reasonable care should know that the same are erroneous. Any Opinion of Counsel may be based, insofar as it relates to factual matters, information with respect to which is in the possession of the Company or any Guarantor, upon the Officer's Certificate of the Company or such Guarantor, as applicable, unless such counsel knows that the Officer's Certificate with respect to the matters upon which his or her Opinion of Counsel may be based as aforesaid are erroneous, or in the exercise of reasonable care should know that the same are erroneous.

Any Officer's Certificate or Opinion of Counsel may be based, insofar as it relates to accounting matters, upon a certificate or opinion of or representations by an accountant or firm of accountants in the employ of the Company or any Guarantor, as applicable, unless such officer or counsel, as the case may be, knows that the certificate or opinion or representations with respect to the accounting matters upon which his or her Officer's Certificate or Opinion of Counsel may be based as aforesaid are erroneous, or in the exercise of reasonable care should know that the same are erroneous.

Any certificate or opinion of any independent firm of public accountants filed with and directed to the Trustee shall contain a statement that such firm is independent.

Section 17.06 *Legal Holidays.* In any case where any Interest Payment Date, Fundamental Change Repurchase Date, Redemption Date or Maturity Date is not a Business Day, then any action to be taken on such date need not be taken on such date, but may be taken on the next succeeding Business Day with the same force and effect as if taken on such date, and no interest shall accrue in respect of the delay.

Section 17.07 *No Security Interest Created.* Nothing in this Indenture or in the Notes, expressed or implied, shall be construed to constitute a security interest under the Uniform Commercial Code or similar legislation, as now or hereafter enacted and in effect, in any jurisdiction.

Section 17.08 *Benefits of Indenture.* Nothing in this Indenture or in the Notes, expressed or implied, shall give to any Person, other than the Holders, the parties hereto, any Paying Agent,

any Exchange Agent, any authenticating agent, any Note Registrar and their successors hereunder, any benefit or any legal or equitable right, remedy or claim under this Indenture.

Section 17.09 *Table of Contents, Headings, Etc.* The table of contents and the titles and headings of the articles and sections of this Indenture have been inserted for convenience of reference only, are not to be considered a part hereof, and shall in no way modify or restrict any of the terms or provisions hereof.

Section 17.10 *Authenticating Agent.* The Trustee may appoint an authenticating agent that shall be authorized to act on its behalf and subject to its direction in the authentication and delivery of Notes in connection with the original issuance thereof and transfers and exchanges of Notes hereunder, including under Section 2.04, Section 2.05, Section 2.06, Section 2.07, Section 10.04 and Section 15.04 as fully to all intents and purposes as though the authenticating agent had been expressly authorized by this Indenture and those Sections to authenticate and deliver Notes. For all purposes of this Indenture, the authentication and delivery of Notes by the authenticating agent shall be deemed to be authentication and delivery of such Notes "by the Trustee" and a certificate of authentication executed on behalf of the Trustee by an authenticating agent shall be deemed to satisfy any requirement hereunder or in the Notes for the Trustee's certificate of authentication. Such authenticating agent shall at all times be a Person eligible to serve as trustee hereunder pursuant to Section 7.08.

Any corporation or other entity into which any authenticating agent may be merged or converted or with which it may be consolidated, or any corporation or other entity resulting from any merger, consolidation or conversion to which any authenticating agent shall be a party, or any corporation or other entity succeeding to the corporate trust business of any authenticating agent, shall be the successor of the authenticating agent hereunder, if such successor corporation or other entity is otherwise eligible under this Section 17.10, without the execution or filing of any paper or any further act on the part of the parties hereto or the authenticating agent or such successor corporation or other entity.

Any authenticating agent may at any time resign by giving written notice of resignation to the Trustee and to the Company. The Trustee may at any time terminate the agency of any authenticating agent by giving written notice of termination to such authenticating agent and to the Company. Upon receiving such a notice of resignation or upon such a termination, or in case at any time any authenticating agent shall cease to be eligible under this Section, the Trustee may appoint a successor authenticating agent (which may be the Trustee), shall give written notice of such appointment to the Company and shall send notice of such appointment to all Holders as the names and addresses of such Holders appear on the Note Register.

The Company agrees to pay to the authenticating agent from time to time reasonable compensation for its services although the Company may terminate the authenticating agent, if it determines such agent's fees to be unreasonable.

The provisions of Section 7.02, Section 7.03, Section 7.04, Section 8.03 and this Section 17.10 shall be applicable to any authenticating agent.

If an authenticating agent is appointed pursuant to this Section 17.10, the Notes may have endorsed thereon, in addition to the Trustee's certificate of authentication, an alternative certificate of authentication in the following form:

> _____,
> as Authenticating Agent, certifies that this is one of the Notes described
> in the within-named Indenture.
>
> By: _____
> Authorized Signatory

Section 17.11 *Execution in Counterparts.* This Indenture may be executed in any number of counterparts, each of which shall be an original, but such counterparts shall together constitute but one and the same instrument. The exchange of copies of this Indenture and of signature pages by facsimile or PDF transmission shall constitute effective execution and delivery of this Indenture as to the parties hereto and may be used in lieu of the original Indenture for all purposes. Signatures of the parties hereto transmitted by facsimile or PDF shall be deemed to be their original signatures for all purposes.

Section 17.12 *Conflict with Trust Indenture Act*. If any provision hereof limits, qualifies or conflicts with another provision hereof which is required to be included in this Indenture by any of the provisions of the Trust Indenture Act, such required provision shall control.

Section 17.13 *Severability.* In the event any provision of this Indenture or in the Notes shall be invalid, illegal or unenforceable, then (to the extent permitted by law) the validity, legality or enforceability of the remaining provisions shall not in any way be affected or impaired.

Section 17.14 *Waiver of Jury Trial.* EACH OF THE COMPANY, THE GUARANTORS AND THE TRUSTEE HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS INDENTURE, THE GUARANTEE, THE NOTES OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THEREBY.

Section 17.15 *Force Majeure.* In no event shall the Trustee be responsible or liable for any failure or delay in the performance of its obligations hereunder arising out of or caused by, directly or indirectly, forces beyond its control, including strikes, work stoppages, accidents, acts of war or terrorism, civil or military disturbances, nuclear or natural catastrophes or acts of God, and interruptions, loss or malfunctions of utilities, communications or computer (software and

hardware) services; it being understood that the Trustee shall use reasonable efforts that are consistent with accepted practices in the banking industry to resume performance as soon as practicable under the circumstances.

Section 17.16 *Calculations*. Except as otherwise provided herein, the Company shall be responsible for making all calculations called for under the Notes. These calculations include, but are not limited to, determinations of the Last Reported Sale Price per Ordinary Share, the Daily VWAPs, the Daily Exchange Values, the Daily Settlement Amounts, any accrued interest payable on the Notes and the Exchange Rate of the Notes. The Company shall make all these calculations in good faith and, absent manifest error, the Company's calculations shall be final and binding on Holders of Notes. The Company shall provide a schedule of its calculations to each of the Trustee and the Exchange Agent, and each of the Trustee and Exchange Agent is entitled to rely conclusively upon the accuracy of the Company's calculations without independent verification (and neither the Trustee nor the Exchange Agent shall have any responsibility for such calculations). The Trustee will forward the Company's calculations to any Holder of Notes upon the written request of that Holder at the sole cost and expense of the Company.

Section 17.17 *U.S.A. Patriot Act.* The parties hereto acknowledge that in accordance with Section 326 of the U.S.A. Patriot Act, the Trustee (in all of its capacities), like all financial institutions and in order to help fight the funding of terrorism and money laundering, is required to obtain, verify, and record information that identifies each person or legal entity that establishes a relationship or opens an account with the Trustee. The parties to this Indenture agree that they will provide the Trustee with such information as it may request in order for the Trustee to satisfy the requirements of the U.S.A. Patriot Act.

Section 17.18 *Tax Withholding.* The Company or the Trustee, as the case may be, shall be entitled to make a deduction or withholding from any payment which it makes under this Indenture for or on account of any present or future taxes, duties or charges if and to the extent so required by any applicable law and any current or future regulations or agreements thereunder or official interpretations thereof or any law implementing an intergovernmental approach thereto or by virtue of the relevant Holder failing to satisfy any certification or other requirements in respect of the Notes, in which event the Company or the Trustee, as the case may be, shall make such payment after such withholding or deduction has been made and shall account to the relevant authorities for the amount so withheld or deducted and shall have no obligation to gross up any payment hereunder or pay any additional amount as a result of such withholding tax.

ARTICLE 18
Subordination

Section 18.01 *Notes Subordinate to Senior Debt.* The Company covenants and agrees, and each Holder of a Note, whether upon original issue or upon transfer, assignment or exchange thereof, by such Holder's acceptance thereof, likewise covenants and agrees, that, notwithstanding anything in this Indenture or the Notes to the contrary, the indebtedness evidenced by the Notes and the payment of the principal of (and premium, if any) and interest on each and all of the Notes are hereby expressly made subordinate and junior in right of payment to the prior payment in full in cash of all Senior Debt, whether outstanding at the date of this Indenture or thereafter incurred, to the extent and in the manner provided in this Indenture.

Section 18.02 *Payment Over of Proceeds Upon Dissolution, Etc.* In the event of (a) any insolvency or bankruptcy case or proceeding, or any receivership, liquidation, reorganization or other similar case or proceeding in connection therewith, relative to the Company, any Guarantor or to their respective creditors, as such, or to their respective assets, or (b) any liquidation, dissolution or other winding up of the Company or any Guarantor, whether voluntary or involuntary and whether or not involving insolvency or bankruptcy, or (c) any assignment for the benefit of creditors or any other marshalling of assets and liabilities of the Company or any Guarantor, then and in any such event the holders of Senior Debt shall be entitled to receive payment in full of all amounts due or to become due on or in respect of all Senior Debt (including any interest accruing thereon after the commencement of any such case or proceeding), or provision shall be made for such payment in cash or cash equivalents or otherwise in a manner satisfactory to the holders of Senior Debt, before the Holders of the Notes are entitled to receive any payment on account of principal of (or premium, if any), interest or other amounts due on the Notes, and to that end the holders of Senior Debt shall be entitled to receive, for application to the payment thereof, any payment or distribution of any kind or character, whether in cash, property or securities, including any such payment or distribution which may be payable or deliverable by reason of the payment of any other indebtedness of the Company or any Guarantor being subordinated to the payment of the Notes, which may be payable or deliverable in respect of the Notes in any such case, proceeding, dissolution, liquidation or other winding up event.

In the event that, notwithstanding the foregoing provisions of this Section, the Trustee or the Holder of any Note shall have received any payment or distribution of assets of the Company or any Guarantor of any kind or character in respect of the Notes, whether in cash, property or securities, including any such payment or distribution which may be payable or deliverable by reason of the payment of any other indebtedness of the Company or any Guarantor being subordinated to the payment of the Notes, before all Senior Debt is paid in full or payment thereof provided for, and if such fact shall, at or prior to the time of such payment or distribution, have been made known to the Trustee in accordance with the terms of Section 18.10 hereof or, as the case may be, such Holder, subject to the terms of Section 18.10 hereof, then and in such

event such payment or distribution shall be paid over or delivered forthwith by the Trustee or such Holder to the trustee in bankruptcy, receiver, liquidating trustee, custodian, assignee, agent or other Person making payment or distribution of assets of the Company or any Guarantor for application to the payment of all Senior Debt remaining unpaid, to the extent necessary to pay all Senior Debt in full, after giving effect to any concurrent payment or distribution to or for the holders of Senior Debt. Any taxes that have been withheld or deducted from any payment or distribution in respect of the Notes, or any taxes that ought to have been withheld or deducted from any such payment or distribution that have been remitted to the relevant taxing authority, shall not be considered to be an amount that the Trustee or the Holder of any Note receives for purposes of this Section 18.02.

For purposes of this Article 18 only, the words "cash, property or securities" shall not be deemed to include shares of stock of the Company as reorganized or readjusted, or securities of the Company or any other corporation or other entity, provided for by a plan of reorganization or readjustment which are subordinated in right of payment to all Senior Debt which may at the time be outstanding to substantially the same extent as, or to a greater extent than, the Notes are so subordinated as provided in this Article 18.

Section 18.03 *Prior Payment to Senior Debt Upon Acceleration of Notes.* In the event that any Notes are declared due and payable before their Maturity Date, the holders of Senior Debt shall be entitled to receive payment in full of all amounts due or to become due on or in respect of all Senior Debt or provision shall be made for such payment in cash, before the Holders of the Notes are entitled to receive any payment (including any payment which may be payable by reason of the payment of any other indebtedness of the Company being subordinated to the payment of the Notes) by the Company on account of the principal of (or premium, if any) or interest or other amounts due on the Notes or on account of the purchase or other acquisition of Notes. In the event that, notwithstanding the foregoing, the Company shall make any payment to the Trustee or the Holder of any Note prohibited by the foregoing provisions of this Section, and if such fact shall, at or prior to the time of such payment, have been made known to the Trustee in accordance with the terms of Section 18.10 hereof or, as the case may be, such Holder, subject to the terms of Section 18.10 hereof, then and in such event such payment shall be paid over and delivered to the Company for application to the payment of all Senior Debt remaining unpaid, to the extent necessary to pay all Senior Debt in full, after giving effect to any concurrent payment or distribution to or for the holders of Senior Debt.

Section 18.04 *No Payment When Senior Debt in Default.* In the event and during the continuation of any default in the payment of principal of (or premium, if any), interest or other amounts due on any Senior Debt beyond any applicable grace period with respect thereto, or in the event that any event of default with respect to any Senior Debt shall have occurred and be continuing permitting the holders of such Senior Debt (or a trustee on behalf of the holders thereof) to declare such Senior Debt due and payable prior to the date on which it would otherwise have become due and payable, unless and until such event of default shall have been

waived in writing and any such declaration and its consequences shall have been rescinded or annulled, or in the event that any judicial proceeding shall be pending with respect to any such default in payment or event of default, or in the event that any event of default with respect to any Senior Debt would result from any payments of the Notes, then no payments (including principal payments, interest payments or, to the extent applicable, any payment which may be payable by reason of the payment of any other indebtedness of the Company being subordinated to the payment of the Note) shall be made by the Company or any Guarantor on the Notes or on account of the purchase or other acquisition of Notes.

In the event that, notwithstanding the foregoing, the Company or any Guarantor shall make any payment to the Trustee or the Holder of any Note prohibited by the provisions of this Section 18.04, and if such fact shall, at or prior to the time of such payment, have been made known to the Trustee in accordance with the terms of Section 18.10 hereof or, as the case may be, such Holder, subject to the terms of Section 18.10 hereof, then and in such event such payment shall be paid over and delivered to the Company for application to the payment of all Senior Debt remaining unpaid, to the extent necessary to pay all Senior Debt in full, after giving effect to any concurrent payment or distribution to or for the holders of Senior Debt. The provisions of this Section shall not apply to any payment with respect to which Section 18.02 would be applicable.

Section 18.05 *Payment Permitted in Certain Situations*. Nothing contained in this Article 18 or elsewhere in this Indenture or in any of the Notes shall prevent, at any time except during the pendency of any case, proceeding, dissolution, liquidation or other winding up, assignment for the benefit of creditors or other marshalling of assets and liabilities of the Company or any Guarantor referred to in Section 18.02 or under the conditions described in Section 18.03 or Section 18.04, (a) the Company from making payments on account of the principal of (or premium, if any) or interest or other amounts due on the Notes, or on account of the purchase or other acquisition of Notes, including pursuant to any Optional Redemption in accordance with Article 16, or (b) the application by the Trustee of any money deposited with it hereunder to the payment of or on account of the principal of (and premium, if any) or interest or other amounts due on the Notes or the retention of such payment by the Holders, if, at the time of such application by the Trustee, it has not received the notice and Company Order required under Section 18.10 hereof.

Section 18.06 *Subrogation to Rights of Holders of Senior Debt.* Subject to the payment in full of all Senior Debt or the provision for such payment in cash or cash equivalents or otherwise in a manner satisfactory to the holders of Senior Debt, the Holders of the Notes shall be subrogated to the extent of the payments or distributions made to the holders of such Senior Debt pursuant to the provisions of this Article 18 (equally and ratably with the holders of indebtedness of the Company which by its express terms is subordinated to indebtedness of the Company to substantially the same extent as the Notes are subordinated to the Senior Debt and is entitled to like rights of subrogation) to the rights of the holders of such Senior Debt to receive

payments and distributions of cash, property and securities applicable to the Senior Debt to the extent that the principal of (and premium, if any) and interest are payable under this Indenture and the Notes. For purposes of such subrogation, no payments or distributions to the holders of the Senior Debt of any cash, property or securities to which the Holders of the Notes or the Trustee would be entitled except for the provisions of this Article 18, and no payments over pursuant to the provisions of this Article 18 to the holders of Senior Debt by Holders of the Notes or the Trustee, shall, as among the Company, its creditors other than holders of Senior Debt and the Holders of the Notes, be deemed to be a payment or distribution by the Company to or on account of the Senior Debt.

Section 18.07 *Provisions Solely to Define Relative Rights.* The provisions of this Article 18 are and are intended solely for the purpose of defining the relative rights of the Holders of the Notes on the one hand and the holders of Senior Debt on the other hand. Nothing contained in this Article 18 is intended to or shall (i) impair, as between the Company and the Holders of the Notes, the obligation of the Company to pay to the Holders of the Notes the principal of (and premium, if any) and interest on the Notes as and when the same shall become due and payable in accordance with their terms or prevent the Trustee or the Holder of any Note from exercising all rights and remedies otherwise permitted by applicable law upon default under this Indenture, subject to the rights of the holders of Senior Debt to receive cash, property and securities otherwise payable or deliverable to the Trustee or such Holder in accordance with this Article 18, (ii) enhance the rights of the Holders of the Notes to the principal of (and premium, if any) and interest on the Notes in accordance with their terms, or (iii) cause any additional principal or interest on the Notes, or other amounts, to be due and payable to the Holders of the Notes.

Section 18.08 *Trustee to Effectuate Subordination*. Each Holder of a Note by such Holder's acceptance thereof authorizes and directs the Trustee on such Holder's behalf to take such action as may be necessary or appropriate to effectuate the subordination provided in this Article 18 and appoints the Trustee as such Holder's attorney-in-fact in connection therewith.

Section 18.09 *No Waiver of Subordination Provisions*. No right of any present or future holder of any Senior Debt to enforce subordination as herein provided shall at any time in any way be prejudiced or impaired by any act or failure to act on the part of the Company or any Guarantor or by any act or failure to act, in good faith, by any such holder, or by any non-compliance by the Company or any Guarantor with the terms, provisions and covenants of this Indenture, regardless of any knowledge thereof any such holder may have or be otherwise charged with. Without in any way limiting the generality of the foregoing paragraph, the holders of Senior Debt may, at any time and from time to time, and in their absolute discretion, change the manner, place or terms of payment or extend the time of payment of, or renew or alter, any such Senior Debt or otherwise amend or supplement in any manner such Senior Debt or any instrument evidencing the same or any agreement under which such Senior Debt is outstanding.

Section 18.10 *Notice to Trustee*. The Company shall give prompt written notice to the Trustee of any fact known to the Company which would prohibit the making of any payment to or by the Trustee in respect of the Notes. Notwithstanding the provisions of this Article or any other provision of this Indenture, the Trustee shall not be charged with knowledge of the existence of any facts which would prohibit the making of any payment to or by the Trustee in respect of the Notes, unless and until the Trustee shall have received written notice thereof from the Company and/or a holder of Senior Debt (or from any trustee therefor) as set forth below; and, prior to the receipt of any such written notice, the Trustee, subject to the provisions of Section 7.01, shall be entitled in all respects to assume that no such facts exist. The Trustee shall make any payment(s) or distribution(s) to the holders of Senior Debt under this Article only upon (i) a Company Order notifying the Trustee of an event under Sections 18.02, 18.03 or 18.04 hereof and directing the Trustee to make such payment(s) or distribution(s) to the holders of Senior Debt or (ii) written notice from a holder of Senior Debt (or a trustee therefor) notifying the Trustee of an event under Section 18.02, 18.03 or 18.04 hereof and directing the Trustee to make such payment(s) or distribution(s) as provided for in such notice, together with a Company Order notifying the Trustee that such holder of Senior Debt (or trustee therefor) is a holder of Senior Debt and is entitled to participate in any such payment(s) or distribution(s) and directing the Trustee to make such payment(s) or distribution(s). Subject to the provisions of Section 7.01 hereof, the Trustee shall be entitled to rely upon any notice, request, instruction, direction, certificate, consent, statement, instrument, document, order or other writing received by it under this Article 18 in order to make any determination hereunder, including, without limitation, any written notice by a Person representing himself to be a holder of Senior Debt (or a trustee therefor) to establish that such notice has been given by a holder of Senior Debt (or a trustee therefor), and shall not incur liability for relying upon any such notice, request, instruction, direction, certificate, consent, statement, instrument, document, order or other writing believed by it to be genuine. The Trustee may consult with legal counsel (who may be counsel for the Company), independent accountants and other experts selected by it in connection with any notice, request, instruction, direction, certificate, consent, statement, instrument, document, order or other writing received by it under this Article 18, and shall not be liable for any action taken or not taken by it in reliance on such consultation. In the event that the Trustee determines in good faith that further evidence is required with respect to the right of any Person as a holder of Senior Debt to participate in any payment or distribution pursuant to this Article 18, the Trustee may request the Company and/or such Person to furnish evidence to the reasonable satisfaction of the Trustee as to the amount of Senior Debt held by such Person, the extent to which such Person is entitled to participate in such payment or distribution and any other facts pertinent to the rights of such Person under this Article 18, and if such evidence is not furnished, the Trustee may defer any payment to such Person pending judicial determination as to the right of such Person to receive such payment.

Section 18.11 *Reliance on Judicial Order or Certificate of Liquidating Agent.* Upon any payment or distribution of assets of the Company or any Guarantor referred to in this Article 18, the Trustee, subject to the provisions of Section 7.01, and the Holders of the Notes shall be

entitled to rely upon any order or decree entered by any court of competent jurisdiction in which such insolvency, bankruptcy, receivership, liquidation, reorganization, dissolution, winding up or similar case or proceeding is pending, or a certificate of the trustee in bankruptcy, receiver, liquidating trustee, custodian, assignee for the benefit of creditors, agent or other Person making such payment or distribution, delivered to the Trustee or to the Holders of Notes, for the purpose of ascertaining whether such payment or distribution is permissible under the terms of this Article 18, including, without limitation for the purpose of ascertaining whether the Persons are entitled to participate in such payment or distribution, the holders of Senior Debt and other indebtedness of the Company, the amount thereof or payable thereon, the amount or amounts paid or distributed thereon and all other facts pertinent thereto or to this Article 18.

Section 18.12 *Trustee Not Fiduciary for Holders of Senior Debt*. The Trustee shall not be deemed to owe any fiduciary duty to the holders of Senior Debt and shall not be liable to any such holders or creditors for any action or omission taken by it under the terms of this Article 18, including, without limitation, for any action or omission taken by it in reliance on any notice, request, instruction, direction, certificate, consent, statement, instrument, document, order or other writing received by it under this Article 18. With respect to the holders of Senior Debt, the Trustee undertakes to perform or to observe only such of its covenants or obligations as are specifically set forth in this Article 18 and no implied covenants or obligations with respect to holders of Senior Debt shall be read into this Indenture against the Trustee. For the avoidance of doubt, (i) when acting under this Article 18, the Trustee shall have all of the rights, benefits, privileges, protections and indemnities provided to the Trustee under Article 7 of this Indenture, and (ii) the Trustee shall not have any duty to take any discretionary action or exercise any discretionary powers in acting under this Article 18.

Section 18.13 *Rights of Trustee as Holder of Senior Debt; Preservation of Trustee's Rights.* The Trustee in its individual capacity shall be entitled to all the rights set forth in this Article 18 with respect to any Senior Debt which may at any time be held by it, to the same extent as any other holder of Senior Debt and nothing in this Indenture shall deprive the Trustee of any of its rights as such holder. Nothing in this Article 18 shall apply to claims of, or payments to, the Trustee under or pursuant to Section 7.06.

Section 18.14 *Article Applicable to Paying Agents.* In case at any time any Paying Agent other than the Trustee shall have been appointed by the Company and be then acting hereunder, the term "Trustee" as used in this Article 18 shall in such case (unless the context otherwise requires) be construed as extending to and including such Paying Agent within its meaning as fully for all intents and purposes as if such Paying Agent were named in this Article 18 in addition to or in place of the Trustee.

Section 18.15 *Modification of Subordination Provisions*. Anything in Article 10 or elsewhere contained in this Indenture to the contrary notwithstanding, no modification or

amendment of this Indenture and no supplemental indenture shall modify the subordination provisions of this Article 18 in a manner that would adversely affect the holders of Senior Debt.

Section 18.16 *Senior Debt Entitled to Rely.* Each holder of a Note, by accepting such Note, acknowledges and agrees that the subordination provisions contained in this Article 18 are, and are intended to be, an inducement and a consideration to each holder of the Senior Debt, whether the Senior Debt was created or acquired before or after the issuance of the Notes, to acquire or continue to hold the Senior Debt, and such holders of the Senior Debt shall have the right to rely upon this Article 18, and no amendment or modification of the provisions contained herein shall diminish the rights of such holders unless such holders shall have agreed in writing thereto. Each holder of a Note, by accepting such Note, and the Trustee, on behalf of the holders of such Notes, hereby waives the benefits, if any, of any statutory or common law rule that may permit a subordinating creditor to assert any defenses of a surety or guarantor, or that may give the subordinating creditor the right to require a senior creditor to marshal assets, and they each agree that it shall not assert any such defenses or rights.

Section 18.17 *Reinstatement.* To the extent the payment of or distribution in respect of the Senior Debt (whether by or on behalf of the Company as proceeds of security or enforcement of any right of setoff or otherwise) is declared to be fraudulent or preferential, set aside or required to be paid to any receiver, trustee in bankruptcy, liquidating trustee, agent or similar Person under any bankruptcy, insolvency, receivership, fraudulent conveyance or similar law, then if such payment or distribution is recovered by, or paid over to, such receiver, trustee in bankruptcy, liquidating trustee, agent or similar Person, the Senior Debt or part thereof originally intended to be satisfied shall be deemed to be reinstated and outstanding as if such payment had not occurred.

Section 18.18 *Action by Holders of Senior Debt.* The holders of the Senior Debt may, at any time and from time to time, without the consent of or notice to the Trustee or the Holders, without incurring responsibility to the Holders and without impairing or releasing the subordination provided in this Indenture or the obligations of the Holders hereunder to the holders of the Senior Debt, take any action deemed appropriate in the sole discretion of the holders of Senior Debt, including, without limitation, doing any one or more of the following:

(i) change the manner, place or terms of payment or extend the time of payment of, or renew or alter, the Senior Debt or any instrument evidencing the same or any agreement under which the Senior Debt is outstanding or secured;

(ii) sell, exchange, release or otherwise deal with any property pledged, mortgaged or otherwise secured;

(iii) release any Person liable in any manner for the collection of the Senior Debt;

(iv) exercise or refrain from exercising any rights against the Company or any other Person; and

(v) take any other action in the reasonable business judgment of the holders of the Senior Debt.

No such action or inaction shall impair or otherwise affect the holder of the Senior Debt's rights under the Notes or this Indenture.

[*Remainder of page intentionally left blank*]

IN WITNESS WHEREOF, the parties hereto have caused this Indenture to be duly executed as of the date first written above.

ITERUM THERAPEUTICS BERMUDA LIMITED, as Notes Issuer

By: /s/ Louise Barrett
Name:Louise Barrett
Title: Director

ITERUM THERAPEUTICS PLC, as Guarantor

By: /s/ David Kelly
Name:David Kelly
Title: Director

ITERUM THERAPEUTICS INTERNATIONAL LIMITED, as Guarantor

By: /s/ Louise Barrett
Name:Louise Barrett
Title: Director

ITERUM THERAPEUTICS U.S. LIMITED, as Guarantor

By: /s/ Judith M. Matthews
Name:Judith M. Matthews
Title: Director

ITERUM THERAPEUTICS U.S. HOLDING LIMITED, as Guarantor

By: /s/ Judith M. Matthews
Name:Judith M. Matthews
Title: Director

U.S. BANK NATIONAL ASSOCIATION, as Trustee

By: /s/ Alicia Pelletier
Name:Alicia Pelletier
Title: Officer

EXHIBIT A

Form of Note

[FORM OF FACE OF NOTE]

THIS NOTE AND THE INDEBTEDNESS EVIDENCED HEREBY ARE, TO THE EXTENT PROVIDED IN THE INDENTURE PURSUANT TO WHICH THIS NOTE IS ISSUED, SUBORDINATE AND SUBJECT IN RIGHT OF PAYMENT TO THE PRIOR PAYMENT IN FULL OF ALL SENIOR DEBT, AND THIS NOTE IS ISSUED SUBJECT TO THE PROVISIONS OF THE INDENTURE WITH RESPECT THERETO. BY ITS ACCEPTANCE HEREOF, EACH HOLDER AND ANY BENEFICIAL OWNER OF THIS NOTE IRREVOCABLY (A) AGREES TO BE BOUND BY SUCH PROVISIONS OF THE INDENTURE, (B) AUTHORIZES AND DIRECTS THE TRUSTEE ON HIS, HER OR ITS BEHALF TO TAKE SUCH ACTIONS AS MAY BE NECESSARY OR APPROPRIATE TO EFFECTUATE THE SUBORDINATION SO PROVIDED, (C) APPOINTS THE TRUSTEE AS HIS, HER OR ITS ATTORNEY-IN-FACT FOR ANY AND ALL SUCH PURPOSES AND (D) WAIVES ALL NOTICE OF THE ACCEPTANCE OF THE SUBORDINATION PROVISIONS CONTAINED HEREIN AND IN THE INDENTURE BY EACH HOLDER OF SENIOR DEBT, WHETHER NOW OUTSTANDING OR HEREAFTER CREATED, INCURRED, ASSUMED OR GUARANTEED, AND WAIVES RELIANCE BY EACH SUCH HOLDER UPON SAID PROVISIONS.

[INCLUDE FOLLOWING LEGEND IF A GLOBAL NOTE]

[UNLESS THIS CERTIFICATE IS PRESENTED BY AN AUTHORIZED REPRESENTATIVE OF THE DEPOSITORY TRUST COMPANY, A NEW YORK CORPORATION ("DTC"), TO THE COMPANY OR ITS AGENT FOR REGISTRATION OF TRANSFER, EXCHANGE, OR PAYMENT, AND ANY CERTIFICATE ISSUED IS REGISTERED IN THE NAME OF CEDE & CO. OR IN SUCH OTHER NAME AS IS REQUESTED BY AN AUTHORIZED REPRESENTATIVE OF DTC (AND ANY PAYMENT HEREUNDER IS MADE TO CEDE & CO. OR TO SUCH OTHER ENTITY AS IS REQUESTED BY AN AUTHORIZED REPRESENTATIVE OF DTC), ANY TRANSFER, PLEDGE, OR OTHER USE HEREOF FOR VALUE OR OTHERWISE BY OR TO ANY PERSON IS WRONGFUL INASMUCH AS THE REGISTERED OWNER HEREOF, CEDE & CO., HAS AN INTEREST HEREIN.]

[INCLUDE FOLLOWING LEGEND IF A RESTRICTED SECURITY]

[THIS SECURITY AND THE ORDINARY SHARES, IF ANY, DELIVERABLE UPON EXCHANGE OF THIS SECURITY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE " **SECURITIES ACT**"), AND MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED EXCEPT IN

ACCORDANCE WITH THE FOLLOWING SENTENCE. BY ITS ACQUISITION HEREOF OR OF A BENEFICIAL INTEREST HEREIN, THE ACQUIRER:

(1) REPRESENTS THAT IT AND ANY ACCOUNT FOR WHICH IT IS ACTING IS AN " ACCREDITED INVESTOR" (WITHIN THE MEANING OF RULE 501 UNDER THE SECURITIES ACT), THAT IT EXERCISES SOLE INVESTMENT DISCRETION WITH RESPECT TO EACH SUCH ACCOUNT, AND THAT IT AND ANY SUCH ACCOUNT IS NOT AN AFFILIATE OF ITERUM THERAPEUTICS BERMUDA LIMITED (THE "**COMPANY**"), ITERUM THERAPEUTICS PLC ("**ITERUM**"), ITERUM THERAPEUTICS INTERNATIONAL LIMITED (THE " **IRISH GUARANTOR**"), ITERUM THERAPEUTICS US LIMITED ("**ITERUM U.S. LIMITED**") OR ITERUM THERAPEUTICS US HOLDING LIMITED (TOGETHER WITH ITERUM, THE IRISH GUARANTOR AND ITERUM U.S. LIMITED, THE "**GUARANTORS**"), AND

(2) AGREES FOR THE BENEFIT OF THE COMPANY AND THE GUARANTORS THAT IT WILL NOT OFFER, SELL, PLEDGE OR OTHERWISE TRANSFER THIS SECURITY OR ANY BENEFICIAL INTEREST HEREIN PRIOR TO THE DATE THAT IS THE LATER OF (X) ONE YEAR AFTER THE LAST ORIGINAL ISSUE DATE HEREOF OR SUCH SHORTER PERIOD OF TIME AS PERMITTED BY RULE 144 UNDER THE SECURITIES ACT OR ANY SUCCESSOR PROVISION THERETO AND (Y) SUCH LATER DATE, IF ANY, AS MAY BE REQUIRED BY APPLICABLE LAW, EXCEPT:

(A) TO ITERUM OR ANY SUBSIDIARY THEREOF (INCLUDING THE COMPANY), OR

(B) PURSUANT TO A REGISTRATION STATEMENT WHICH HAS BECOME EFFECTIVE UNDER THE SECURITIES ACT, OR

(C) TO A QUALIFIED INSTITUTIONAL BUYER IN COMPLIANCE WITH RULE 144A UNDER THE SECURITIES ACT, OR

(D) PURSUANT TO AN EXEMPTION FROM REGISTRATION PROVIDED BY RULE 144 UNDER THE SECURITIES ACT (IF AVAILABLE) OR ANY OTHER AVAILABLE EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

PRIOR TO THE REGISTRATION OF ANY TRANSFER IN ACCORDANCE WITH CLAUSE (2)(D) ABOVE, THE COMPANY, THE GUARANTORS AND THE TRUSTEE RESERVE THE RIGHT TO REQUIRE THE DELIVERY OF SUCH LEGAL OPINIONS, CERTIFICATIONS OR OTHER EVIDENCE AS MAY REASONABLY BE REQUIRED IN ORDER TO DETERMINE THAT THE PROPOSED TRANSFER IS BEING MADE IN COMPLIANCE WITH THE SECURITIES ACT AND APPLICABLE STATE SECURITIES LAWS. NO REPRESENTATION IS MADE AS TO THE AVAILABILITY OF ANY EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

THE HOLDER OF THIS SECURITY IS ENTITLED TO THE BENEFITS OF A INVESTOR RIGHTS AGREEMENT (AS SUCH TERM IS DEFINED IN THE INDENTURE REFERRED TO ON THE REVERSE HEREOF) AND, BY ITS ACCEPTANCE HEREOF, AGREES TO BE BOUND BY AND TO COMPLY WITH THE PROVISIONS OF SUCH INVESTOR RIGHTS AGREEMENT.]

Iterum Therapeutics Bermuda Limited

6.500% Exchangeable Senior Subordinated Note due 2025

FOR PURPOSES OF SECTIONS 1272, 1273 AND 1275 OF THE U.S. INTERNAL REVENUE CODE OF 1986, AS AMENDED, THIS NOTE IS BEING ISSUED WITH ORIGINAL ISSUE DISCOUNT. THE ISSUE PRICE OF EACH NOTE IS $768.73, AND THE ISSUE DATE IS [_____]. A HOLDER OF NOTES MAY OBTAIN THE AMOUNT OF ORIGINAL ISSUE DISCOUNT AND YIELD TO MATURITY BY SUBMITTING A WRITTEN REQUEST FOR IT TO THE COMPANY AT THE FOLLOWING ADDRESS: ITERUM THERAPEUTICS PLC, BLOCK 2, FLOOR 3 HARCOURT CENTRE, HARCOURT STREET, DUBLIN 2, IRELAND, ATTENTION: COREY FISHMAN, WITH A COPY TO ITERUM THERAPEUTICS PLC, LEGAL DEPARTMENT, BLOCK 2, FLOOR 3 HARCOURT CENTRE, HARCOURT STREET, DUBLIN 2, IRELAND.

Certificate No. [_____] [Initially][1] $[_____]

[CUSIP No. [•]]

[ISIN No. [•]]

Iterum Therapeutics Bermuda Limited, a company formed under the laws of Bermuda (the "**Company**," which term includes any successor corporation or other entity under the Indenture referred to on the reverse hereof), for value received hereby promises to pay to [CEDE & CO.][2] [_____][3], or registered assigns, the principal sum [as set forth in the "Schedule of Exchanges of Notes" attached hereto][4] [of $[_____]][5], which amount, taken together with the principal amounts of all other outstanding Notes, shall not, unless permitted by the Indenture, exceed $60,000,000 in aggregate at any time, in accordance with the rules and procedures of the Depositary, on January 31, 2025, and interest thereon as set forth below. The Notes will be fully and unconditionally guaranteed by Iterum Therapeutics plc, a company formed under the laws of Ireland ("**Iterum**"), Iterum Therapeutics International Limited, a company formed under the laws of Ireland (the "**Irish Guarantor**"), Iterum Therapeutics US Limited, a Delaware corporation ("**Iterum U.S. Limited**"), Iterum Therapeutics US Holding Limited, a Delaware corporation ("**Iterum U.S. Holding**" and, together with Iterum, the Irish Guarantor and Iterum U.S. Limited, the "**Guarantors**"), on a senior unsecured basis, in accordance with the provisions of Article 13 of the Indenture. Notwithstanding anything in this Note to the contrary, the guarantee of the Note by the Guarantors is subordinate in right of payment to any Guarantor Senior Debt to the extent and in the manner provided in the Indenture, and by its acceptance

[1] Include if a global note.
[2] Include if a global note.
[3] Include if a physical note.
[4] Include if a global note.
[5] Include if a physical note.

hereof, each Holder and any beneficial owner of this Note irrevocably agrees to be bound by such provisions of the Indenture.

This Note shall bear simple, non-compounding interest at the rate of 6.500% per year from [_____],[6] to, but excluding, January 31, 2025, unless earlier repurchased or exchanged pursuant to and in accordance with the provisions of the Indenture. Any interest on this Note shall be computed on the basis of a 360-day year composed of twelve 30-day months and, for partial months, on the basis of actual days elapsed over a 30-day month. All interest on this Note is payable solely on January 31, 2025 to Holders of record at the close of business on January 15, 2025 (whether or not such day is a Business Day), respectively, unless the Notes are earlier repurchased, redeemed or exchanged pursuant to and in accordance with the Indenture. Special Interest will be payable as set forth in Section 6.03 of the within-mentioned Indenture, and any reference to interest on, or in respect of, any Note therein shall be deemed to include Special Interest if, in such context, Special Interest is, was or would be payable pursuant to Section 6.03 or to any interest on any Defaulted Amounts payable as set forth in Section 2.03(c) of the within-mentioned Indenture.

Any Defaulted Amounts shall accrue simple, non-compounding interest per annum at the rate borne by the Notes from, and including, the relevant payment date to, but excluding, the date on which such Defaulted Amounts shall have been paid by the Company, at its election, in accordance with Section 2.03(c) of the Indenture.

The Company shall pay the principal of and interest, if any, on this Note, if and so long as such Note is a Global Note, in immediately available funds in lawful money of the United States at the time to the Depositary or its nominee, as the case may be, as the registered Holder of such Note. As provided in and subject to the provisions of the Indenture, the Company shall pay the principal of any Notes (other than Notes that are Global Notes) at the office or agency designated by the Company for that purpose. The Company has initially designated the Trustee as its Paying Agent, Exchange Agent and Note Registrar in respect of the Notes and its Corporate Trust Office located in the United States of America as a place where Notes may be presented for payment or for registration of transfer and exchange.

Reference is made to the further provisions of this Note set forth on the reverse hereof, including provisions giving the Holder of this Note the right to exchange this Note into cash, Ordinary Shares or a combination of cash and Ordinary Shares, as applicable, on the terms and subject to the limitations set forth in the Indenture. Such further provisions shall for all purposes have the same effect as though fully set forth at this place.

This Note, and any claim, controversy or dispute arising under or related to this Note, shall be construed in accordance with and governed by the laws of the State of New York (without regard to the conflicts of laws provisions thereof).

[6] Insert date of original issuance.

In the case of any conflict between this Note and the Indenture, the provisions of the Indenture shall control and govern.

This Note shall not be valid or become obligatory for any purpose until the certificate of authentication hereon shall have been signed manually or by facsimile by the Trustee or a duly authorized authenticating agent under the Indenture.

[*Remainder of page intentionally left blank*]

IN WITNESS WHEREOF, the Company has caused this Note to be duly executed.

ITERUM THERAPEUTICS BERMUDA LIMITED

By: _____
Name:
Title:

Dated:

TRUSTEE'S CERTIFICATE OF AUTHENTICATION

U.S. BANK NATIONAL ASSOCIATION
as Trustee, certifies that this is one of the Notes described in the within-named Indenture.

By:_____
Authorized Signatory

[FORM OF REVERSE OF NOTE]

Iterum Therapeutics Bermuda Limited

6.500% Exchangeable Senior Subordinated Note due 2025

This Note is one of a duly authorized issue of Notes of the Company, designated as its 6.500% Exchangeable Senior Subordinated Notes due 2025 (the "**Notes**"), limited to the aggregate principal amount of $60,000,000, all issued or to be issued under and pursuant to an Indenture dated as of January 21, 2020 (the "**Indenture**"), among the Company, the Guarantors and U.S. Bank National Association, a national banking association (the "**Trustee**"), to which Indenture and all indentures supplemental thereto reference is hereby made for a description of the rights, limitations of rights, obligations, duties and immunities thereunder of the Trustee, the Company, the Guarantors and the Holders of the Notes. Additional Notes may be issued subject to certain conditions specified in the Indenture. Capitalized terms used in this Note and not defined in this Note shall have the respective meanings set forth in the Indenture.

In case certain Events of Default, as defined in the Indenture, shall have occurred and be continuing, the principal of, and any interest on, all Notes may be declared, by either the Trustee or Holders of at least 25% in aggregate principal amount of Notes then outstanding, and upon said declaration shall become, due and payable, in the manner, with the effect and subject to the conditions and certain exceptions set forth in the Indenture.

Subject to the terms and conditions of the Indenture, the Company will make all payments and deliveries in respect of the Fundamental Change Repurchase Price on the Fundamental Change Repurchase Date, the Redemption Price on the relevant Redemption Date and the principal amount and accrued and unpaid interest on the Maturity Date, as the case may be, to the Holder who surrenders a Note to a Paying Agent to collect such payments in respect of the Note. The Company will pay cash amounts in money of the United States that at the time of payment is legal tender for payment of public and private debts.

The Indenture contains provisions permitting the Company, the Guarantors and the Trustee in certain circumstances, without the consent of the Holders of the Notes, and in certain other circumstances, with the consent of the Holders of not less than the Specified Percentage in aggregate principal amount of the Notes at the time outstanding, evidenced as in the Indenture provided, to execute supplemental indentures modifying the terms of the Indenture and the Notes as described therein. It is also provided in the Indenture that, subject to certain exceptions, the Holders of the Specified Percentage in aggregate principal amount of the Notes at the time outstanding may on behalf of the Holders of all of the Notes waive any past Default or Event of Default under the Indenture and its consequences.

Each Holder shall have the right to receive payment or delivery, as the case may be, of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, any accrued and unpaid interest on, and the consideration due upon exchange of,

this Note at the place, at the respective times, at the rate and in the lawful money (or, if applicable, Ordinary Shares) herein prescribed.

The Notes are issuable in registered form without coupons in minimum denominations of $1,000 principal amount and multiples of $1,000 in excess thereof. At the office or agency of the Company referred to on the face hereof, and in the manner and subject to the limitations provided in the Indenture, Notes may be exchanged for a like aggregate principal amount of Notes of other authorized denominations, without payment of any service charge but, if required by the Company or Trustee, with payment of a sum sufficient to cover any transfer or similar tax that may be imposed in connection therewith as a result of the name of the Holder of the new Notes issued upon such exchange of Notes being different from the name of the Holder of the old Notes surrendered for such exchange.

The Notes shall be redeemable for cash at the Company's option in accordance with the terms and subject to the conditions specified in the Indenture. No sinking fund is provided for the Notes.

Upon the occurrence of a Fundamental Change, the Holder has the right, at such Holder's option, to require the Company to repurchase for cash all of such Holder's Notes or any portion thereof (in minimum principal amounts of $1,000 or multiples of $1,000 in excess thereof) on the Fundamental Change Repurchase Date at a price equal to the Fundamental Change Repurchase Price.

Subject to the provisions of the Indenture, the Holder hereof has the right, at its option, during certain periods and subject to certain conditions specified in the Indenture, prior to the close of business on the second Scheduled Trading Day immediately preceding January 15, 2025 and prior to the date of a Mandatory Exchange Notice, to exchange any Notes or portion thereof that is $1,000 or a multiple of $1,000 in excess thereof, for cash, Ordinary Shares or a combination of cash and Ordinary Shares, as applicable (such settlement method to be determined at the election of the Company), at the Exchange Rate specified in the Indenture, as adjusted from time to time as provided in the Indenture.

Subject to the provisions of the Indenture, upon a Mandatory Exchange, this Note will be automatically exchanged for cash, Ordinary Shares or a combination of cash and Ordinary Shares, as applicable, at the Exchange Rate specified in the Indenture, as adjusted from time to time as provided in the Indenture.

Terms used in this Note and defined in the Indenture are used herein as therein defined.

ABBREVIATIONS

The following abbreviations, when used in the inscription of the face of this Note, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM = as tenants in common

UNIF GIFT MIN ACT = Uniform Gifts to Minors Act

CUST = Custodian

TEN ENT = as tenants by the entireties

JT TEN = joint tenants with right of survivorship and not as tenants in common
Additional abbreviations may also be used though not in the above list.

SCHEDULE A[7]

SCHEDULE OF EXCHANGES OF NOTES

Iterum Therapeutics Bermuda Limited

6.500% Exchangeable Senior Subordinated Notes due 2025

The initial principal amount of this Global Note is _____ DOLLARS ($_____). The following increases or decreases in this Global Note have been made:

Date of exchange	Amount of decrease in principal amount of this Global Note	Amount of increase in principal amount of this Global Note	Principal amount of this Global Note following such decrease or increase	Signature of authorized signatory of Trustee or Custodian

7 Include if a global note.

ATTACHMENT 1

[FORM OF NOTICE OF EXCHANGE]

To: U.S. Bank National Association, as Exchange Agent

The undersigned registered owner of this Note hereby exercises the option to exchange this Note, or the portion hereof (that is $1,000 principal amount or a multiple thereof) below designated, for cash, Ordinary Shares or a combination of cash and Ordinary Shares, as applicable, in accordance with the terms of the Indenture referred to in this Note, and directs that any cash payable and any Ordinary Shares issuable and deliverable upon such exchange, together with any cash for any fractional share, and any Notes representing any unexchanged principal amount hereof, be issued and delivered to the registered Holder hereof unless a different name has been indicated below. If any Ordinary Shares or any portion of this Note not exchanged are to be issued in the name of a Person other than the undersigned, the undersigned will pay all documentary, stamp or similar issue or transfer taxes, if any in accordance with Section 14.02(d) and Section 14.02(e) of the Indenture. Any amount required to be paid to the undersigned on account of any interest accompanies this Note.

If the undersigned is a Holder of a Specified Note, the undersigned (i) represents and warrants that the exchange of this Note, or the portion thereof below designated, and the issuance of cash, Ordinary Shares or a combination of cash and Ordinary Shares upon such exchange, may be done in compliance with the restrictions set forth in Section 14.01(c) of the Indenture and (ii) agrees to provide the Company and the Trustee with any certifications, representations and other documentation reasonably requested by the Company, Iterum or the Trustee to demonstrate the Holder's compliance with Section 14.01(c) of the Indenture.

Dated: _____

_____
Signature(s)

_____
Signature Guarantee

Signature(s) must be guaranteed
by an eligible Guarantor Institution
(banks, stock brokers, savings and
loan associations and credit unions)
with membership in an approved

signature guarantee medallion program
pursuant to Securities and Exchange
Commission Rule 17Ad-15 if Ordinary Shares are to be issued, or
Notes are to be delivered, other than
to and in the name of the registered holder.

Fill in for registration of shares if
to be issued, and Notes if to
be delivered, other than to and in the
name of the registered holder:

_____
(Name)

_____
(Street Address)

_____
(City, State and Zip Code)
Please print name and address

Principal amount to be exchanged (if less than all): $_____,000

NOTICE: The above signature(s) of the Holder(s) hereof must correspond with the name as written upon the face of the Note in every particular without alteration or enlargement or any change whatever.

_____
Social Security or Other Taxpayer
Identification Number

ATTACHMENT 2

[FORM OF FUNDAMENTAL CHANGE REPURCHASE NOTICE]

To: U.S. Bank National Association, as Paying Agent

The undersigned registered owner of this Note hereby acknowledges receipt of a notice from Iterum Therapeutics Bermuda Limited (the "**Company**") as to the occurrence of a Fundamental Change and specifying the Fundamental Change Repurchase Date and requests and instructs the Company to pay to the registered holder hereof in accordance with Section 15.02 of the Indenture referred to in this Note the entire principal amount of this Note, or the portion thereof (that is $1,000 principal amount or a multiple thereof) below designated and any accrued and unpaid interest thereon. Capitalized terms used herein but not defined shall have the meanings ascribed to such terms in the Indenture.

In the case of Physical Notes, the certificate numbers of the Notes to be repurchased are as set forth below:

Dated: _____

_____
Signature(s)

_____
Social Security or Other Taxpayer
Identification Number

Principal amount to be repurchased (if less than all): $_____,000

NOTICE: The above signature(s) of the Holder(s) hereof must correspond with the name as written upon the face of the Note in every particular without alteration or enlargement or any change whatever.

ATTACHMENT 3

[FORM OF ASSIGNMENT AND TRANSFER]

To: U.S. Bank National Association, as Note Registrar

For value received _____ hereby sell(s), assign(s) and transfer(s) unto _____ (Please insert social security or Taxpayer Identification Number of assignee) the within Note, and hereby irrevocably constitutes and appoints _____ attorney to transfer the said Note on the books of the Company, with full power of substitution in the premises.

In connection with any transfer of the within Note occurring prior to the Resale Restriction Termination Date, as defined in the Indenture governing such Note, the undersigned confirms that such Note is being transferred, subject to the terms of the indenture:

□ To Iterum Therapeutics plc or a subsidiary thereof (including Iterum Therapeutics Bermuda Limited); or

□ Pursuant to a registration statement that has become or been declared effective under the Securities Act of 1933, as amended; or

□ Pursuant to and in compliance with Rule 144A under the Securities Act of 1933, as amended; or

□ Pursuant to and in compliance with Rule 144 under the Securities Act of 1933, as amended, or any other available exemption from the registration requirements of the Securities Act of 1933, as amended.

Dated: _____

_____

_____
Signature(s)

_____
Signature Guarantee

Signature(s) must be guaranteed by an eligible Guarantor Institution (banks, stock brokers, savings and loan associations and credit unions) with membership in an approved signature guarantee medallion program pursuant to Securities and Exchange Commission Rule 17Ad-15 if Notes are to be delivered, other than to and in the name of the registered holder.

NOTICE: The signature on the assignment must correspond with the name as written upon the face of the Note in every particular without alteration or enlargement or any change whatever.

EXHIBIT 4.4

ITERUM THERAPEUTICS BERMUDA LIMITED
as Notes Issuer

AND

ITERUM THERAPEUTICS PLC,
ITERUM THERAPEUTICS INTERNATIONAL LIMITED,
ITERUM THERAPEUTICS US LIMITED, and
ITERUM THERAPEUTICS US HOLDING LIMITED
as Guarantors

AND

ITERUM HOLDERS' REPRESENTATIVE LLC,
as Holders' Representative,

AND

COMPUTERSHARE TRUST COMPANY, N.A.,
as Trustee

INDENTURE

Dated as of January 21, 2020

Limited Recourse Royalty-Linked Subordinated Notes

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EXHIBIT

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Reconciliation and tie between Trust Indenture Act of 1939 and Indenture, dated as of January 21, 2020.

Trust Indenture Act Section		Agreement Section
Section 310	(a)(1)	7.08
	(a)(2)	7.08
	(a)(3)	Not Applicable
	(a)(4)	Not Applicable
	(a)(5)	7.08
	(b)	7.09, 7.13
	(c)	Not Applicable
Section 311	(a)	7.14
	(b)	7.14
	(c)	Not Applicable
Section 312	(a)	5.01, 5.02(a)
	(b)	5.02(b)
	(c)	5.02(c)
Section 313	(a)	5.03(a)
	(b)	5.03(a)
	(c)	5.03(a), 6.08(b)
	(d)	5.03(b)
Section 314	(a)	4.09, 5.04
	(b)	Not Applicable
	(c)(1)	2.04, 2.05, 2.10, 3.01, 4.04(e), 7.02, 7.07, 10.05, 11.03, 15.05
	(c)(2)	2.10, 3.01, 7.02, 10.05, 11.03, 15.05
	(c)(3)	Not Applicable
	(d)	Not Applicable
	(e)	15.05
	(f)	Not Applicable
Section 315	(a)	7.01(a), 7.02
	(b)	6.08(b)
	(c)	7.01
	(d)	7.01
	(d)(1)	7.01(a)
	(d)(2)	7.01(b)
	(d)(3)	7.01(c)
	(e)	6.09
Section 316	(a)(last sentence)	8.04
	(a)(1)(A)	6.07

Trust Indenture Act Section		Agreement Section
	(a)(1)(B)	6.07
	(a)(2)	Not Applicable
	(b)	6.04, 6.07
	(c)	8.01
Section 317	(a)(1)	6.02
	(a)(2)	6.02
	(b)	4.04
Section 318	(a)	15.12

Note: This reconciliation and tie shall not, for any purpose, be deemed to be a part of this Indenture.

INDENTURE, dated as of January 21, 2020 , between Iterum Therapeutics Bermuda Limited, a company formed under the laws of Bermuda, as Notes issuer (the "**Company**", as more fully set forth in Section 1.01), ITERUM THERAPEUTICS PLC, a company formed under the laws of Ireland, as guarantor (the "**Parent Guarantor**", as more fully set forth in Section 1.01), Iterum Therapeutics International Limited, a company formed under the laws of Ireland, as guarantor (the "**Irish Guarantor**"), Iterum Therapeutics US Limited, a Delaware corporation, as guarantor ("**Iterum U.S. Limited**"), Iterum Therapeutics US Holding Limited, a Delaware corporation, as guarantor ("**Iterum U.S. Holding**" and, together with Parent Guarantor, the Irish Guarantor, Iterum U.S. Limited and any guarantor added pursuant to a supplemental indenture in accordance with Section 10.01(c) hereof, the "**Guarantors**"), Iterum Holders' Representative LLC, a Delaware limited liability company, as the representative of the noteholders hereunder (the "**Holders' Representative**", as more fully set forth in Section 1.01) and Computershare Trust Company, N.A., as trustee (the "**Trustee**", as more fully set forth in Section 1.01). The Irish Guarantor, Iterum U.S. Limited and Iterum U.S. Holding are referred to herein collectively as the "**Subsidiary Guarantors**".

W I T N E S S E T H:

WHEREAS, as additional consideration for the financing provided to the Company in connection with the issuance of the Exchangeable Senior Subordinated Notes, for its lawful corporate purposes, the Company has duly authorized the issuance of its Limited Recourse Royalty-Linked Subordinated Notes (the "**Notes**"), initially in an aggregate principal amount not to exceed $120,000, and the Guarantors have duly authorized their issuance of the Guarantee, and in order to provide the terms and conditions upon which the Notes are to be authenticated, issued and delivered, the Company and the Parent Guarantor have duly authorized the execution and delivery of this Indenture;

WHEREAS, the Form of Note, the certificate of authentication to be borne by each Note and the Form of Assignment and Transfer to be borne by the Notes are to be substantially in the forms hereinafter provided; and

WHEREAS, all acts and things necessary to make the Notes, when executed by the Company and authenticated and delivered by the Trustee or a duly authorized authenticating agent, as provided in this Indenture, the valid, binding and legal obligations of the Company and the Guarantors, and this Indenture a valid agreement according to its terms, have been done and performed, and the execution of this Indenture and the issuance hereunder of the Notes and the Guarantee have in all respects been duly authorized.

NOW, THEREFORE, THIS INDENTURE WITNESSETH:

That in order to declare the terms and conditions upon which the Notes are, and are to be, authenticated, issued and delivered, and in consideration of the premises and of the purchase and acceptance of the Notes by the Holders thereof, each of the Company and the Guarantors

covenants and agrees with the Trustee for the equal and proportionate benefit of the respective Holders from time to time of the Notes (except as otherwise provided below), as follows:

ARTICLE 1
DEFINITIONS

Section 1.01. *Definitions.* For all purposes of this Indenture, except as expressly provided herein or unless the context otherwise requires:

(a) the terms defined in this Section 1.01 (except as herein otherwise expressly provided or unless the context otherwise requires) for all purposes of this Indenture and of any indenture supplemental hereto shall have the respective meanings specified in this Section 1.01;

(b) all other terms used in this Indenture that are defined in the Trust Indenture Act or the definitions of which in the Securities Act are referred to in the Trust Indenture Act, including terms defined therein by reference to the Securities Act (except as herein otherwise expressly provided or unless the context otherwise clearly requires), shall have the meanings assigned to such terms in the Trust Indenture Act and in the Securities Act as in force at the date of this Indenture;

(c) the words "herein," "hereof," "hereunder," and words of similar import refer to this Indenture as a whole and not to any particular Article, Section or other subdivision;

(d) unless the context otherwise requires, "or" is not inclusive and "including" means "including without limitation"; and

(e) the terms defined in this Article include the plural as well as the singular.

"**Accounting Standards**" means GAAP and, to the extent consistent therewith, the accounting policies and practices of the Parent Guarantor.

"**Acquiring Person**" means any Person, determined from time to time, that has publicly announced an intention to undertake a Change of Control of the Parent Guarantor, or has entered into discussions or negotiations with, or delivered any written letter or notice to, management of Parent Guarantor or any member of the Board of Directors of Parent Guarantor with respect to a Change of Control of the Parent Guarantor, in each case at any time during the twelve month period prior to such determination.

"**Affiliate**" of any specified Person means any other Person directly or indirectly controlling or controlled by or under direct or indirect common control with such specified Person. For the purposes of this definition, "control," when used with respect to any specified Person means the power to direct or cause the direction of the management and policies of such Person, directly or indirectly, whether through the ownership of voting securities, by contract or otherwise; and the terms "controlling" and "controlled" have meanings correlative to the foregoing.

"**Aggregate Maximum Return Amount**" means, as to all Notes then outstanding collectively, the product of 4,000 and the Aggregate Principal Amount.

"**Aggregate Maximum Return Amount Qualification**" shall have the meaning specified in Section 2.03(b).

"**Aggregate Principal Amount**" means the Principal Amounts in respect of all Notes then outstanding collectively, up to the aggregate amount of $120,000.

"**Bankruptcy Code**" means Title 11 of the United States Code.

"**Bankruptcy Law**" means the Bankruptcy Code (or any successor thereto) or any similar bankruptcy, insolvency or other U.S. federal or state law, or similar foreign law (including under Bermudan or Irish law), for the relief of debtors, whether now or hereafter in effect.

"**Benefited Party**" shall have the meaning specified in Section 13.01(b).

"**Board of Directors**" means, with respect to the Company or any Guarantor, the board of directors (or equivalent governing body) of the Company or such Guarantor, as the case may be, or a committee of such board duly authorized to act for it hereunder.

"**Board Resolution**" means a copy of a resolution certified by the Secretary or an Assistant Secretary of the Company or any Guarantor, as the case may be, to have been duly adopted by the applicable Board of Directors, and to be in full force and effect on the date of such certification, and delivered to the Trustee.

"**Business Day**" means, with respect to any Note, any day other than a Saturday, a Sunday or a day on which the Federal Reserve Bank of New York or banking institutions in London, Bermuda or the city in which the Corporate Trust Office is located are authorized or required by law or executive order to close or be closed.

"**Capital Stock**" means, for any Person, any and all shares, interests, rights to purchase, warrants, options, participations or other equivalents of or interests in (however designated) stock or shares issued by that Person, but excluding any debt securities convertible or exchangeable into such stock or shares.

"**Change of Control**" means, with respect to any Person, (i) any method, transaction or series of related transactions by which more than 50% of the outstanding shares of such Person entitled to vote in the election of directors (or, if such Person has outstanding other equity securities entitling the holder thereof to vote in the election of directors, such number and type of equity securities as represent a majority of the voting power of all voting equity securities of such Person) or the beneficial ownership thereof are acquired by a person or group (as defined in Section 13(d) of the Exchange Act); (ii) a merger or consolidation of such Person in which such Person is not the continuing or surviving entity or in which the equityholders of such Person

immediately before such transaction do not own in the aggregate at least 50% of the outstanding voting equity securities of the continuing or surviving entity immediately after such transaction; (iii) a merger or consolidation of such Person pursuant to which such Person's outstanding equity securities are converted into cash, securities or other property; or (iv) a sale of all or substantially all of such Person's consolidated assets.

"**close of business**" means 5:00 p.m. (New York City time).

"**Code**" shall have the meaning specified in Section 4.10(b).

"**Commission**" means the U.S. Securities and Exchange Commission, as from time to time constituted, created under the Exchange Act, or if at any time after the execution and delivery of this Indenture such Commission is not existing and performing the duties now assigned to it under the Trust Indenture Act, then the body performing such duties on such date.

"**Company**" shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns. To the extent necessary to comply with the requirements of the provisions of Trust Indenture Act Sections 310 through 317, inclusive, to the extent that they are applicable to the Company, the term "Company" shall include any other obligor with respect to the Notes for the purposes of complying with such provisions.

"**Company Order**" means a written order of the Company, signed by (a) the Company's Chief Executive Officer, Chief Financial Officer or President or any director of the Company, and (b) any such other Officer designated in clause (a) of this definition or the Company's Secretary or any Assistant Secretary, and delivered to the Trustee.

"**Confidential Information**" shall have the meaning specified in Section 4.12.

"**Corporate Trust Office**" means the designated office of the Trustee at which at any time its corporate trust business shall be administered, which office at the date hereof is Computershare Trust Company, N.A., 8742 Lucent Boulevard, Suite 225, Highlands Ranch, CO 80129, Attention: Corporate Trust Office, or such other address as the Trustee may designate from time to time by notice to the Holders and the Company, or the designated corporate trust office of any successor trustee (or such other address as such successor trustee may designate from time to time by notice to the Holders and the Company).

"**Custodian**" means the Trustee, as custodian for The Depository Trust Company, with respect to the Global Notes, or any successor entity thereto.

"**cUTI Indication**" means the complicated urinary tract infection indication;

"**cUTI Indication Payment Rate**" means 0.00025%; provided, that if the aggregate Principal Amounts in respect of all Notes issued and outstanding immediately after completion of the Rights Offering exceeds $80,000, the cUTI Indication Payment Rate means 0.00025%

multiplied by a fraction, the numerator of which is $80,000, and the denominator of which is the aggregate Principal Amounts in respect of all Notes issued and outstanding immediately after completion of the Rights Offering.

"**Default Interest**" shall have the meaning set forth in Section 2.03(d).

"**Default Rate**" means (i) with respect to Default Interest due pursuant to Section 2.03(d)(i), a per annum rate equal, as of any date that Default Interest accrues, to the prime rate of interest quoted by Bloomberg on such date or on the most recent date when available from Bloomberg, or if not generally available from Bloomberg quoted by a similar reputable data source on such date or on the most recent date quoted, plus three percent (3.00%), and (ii) with respect to Default Interest due pursuant to Section 2.03(d)(ii), a per annum rate equal to four percent (4.00%), in case of clauses (i) and (ii) calculated daily on the basis of a three hundred sixty five (365) day year or, if lower, the highest rate permitted under applicable law.

"**Defaulted Amounts**" means any amounts on any Note that are due and payable but have not been paid or duly provided for.

"**Depositary**" means, with respect to each Global Note, the Person specified in Section 2.05(c) as the Depositary with respect to such Notes, until a successor shall have been appointed and become such pursuant to the applicable provisions of this Indenture, and thereafter, "**Depositary**" shall mean or include such successor.

"**Designated Default Interest**" means Default Interest that becomes due pursuant to Section 2.03(d)(ii) with respect to an Uncurable Event of Default.

"**Diligent Efforts**" means, with respect to a Person and a Product, that level of efforts and resources commonly devoted by a company of similar size and resources to Parent in the research-based pharmaceutical industry, to the development or commercialization, as the case may be, of a product of similar commercial potential at a similar stage in its lifecycle, in each case taking into account issues of safety and efficacy, product profile, the proprietary position, the then-current competitive environment for such product and the likely timing of such product's entry into the market, the regulatory environment and the status of such product, profitability (including pricing and reimbursement) and other relevant scientific, technical, regulatory and commercial factors. Subject to the foregoing, "Diligent Efforts" shall include, but shall not be limited to, the following: (a) making expenditures in relation to a Product that are consistent with expenditures normally made by persons in the pharmaceutical business in connection with products of similar market potential at similar stages in their development or product life; (b) pursuing development of each Product and regulatory approvals to market each Product, including designing and conducting all clinical trials necessary to support applications for regulatory approval; (c) launching and marketing Products in a manner which maximizes Net Revenues; (d) implementing and maintaining appropriate Product and patient support services (including, but not limited to, appropriate risk identification and minimization programs and reimbursement support services); (e) using commercially reasonable efforts to initiate and

complete all appropriate post-marketing approval commitments; (f) promptly seeking pricing approvals and reimbursements; (g) setting or seeking a commercial price for a Product that is consistent with the profile of such Product, including, where appropriate, seeking premium pricing based on the effectiveness of such Product; (h) promoting the Product for all labeled applicable indications; (i) maintaining compliance with all healthcare laws and regulations, and the codes of compliance published by the Pharmaceutical Research and Manufacturers of America; (j) maintaining and enforcing all material intellectual property related to each of the Products; (k) avoiding infringement of any intellectual property rights of third parties; and (k) otherwise fulfilling the obligations of the Guarantors and their Affiliates under the Pfizer License, in order to maintain the rights to develop and commercialize a Product granted thereunder, in each case to the extent such actions are reasonably likely to result in the generation of Net Revenues.

"**ECI**" shall have the meaning set forth in Section 4.10(f).

"**End Date**" means December 31, 2045, or, in the event that no FDA Approvals have been obtained prior to December 31, 2025, such date.

"**Event of Default**" shall have the meaning specified in Section 6.01.

"**Exchange Act**" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

"**Exchangeable Senior Subordinated Notes**" means the 6.500% Exchangeable Senior Subordinated Notes due 2025 issued under an Indenture, dated on or about the date hereof, among the Company, as issuer, the Guarantors, as guarantors, and U.S. Bank National Association, as trustee.

"**FDA**" means the United States Food and Drug Administration or any successor federal agency thereto.

"**FDA Approval**" means receipt by the Parent Guarantor (or a Subsidiary thereof) of approval of a new drug application and/or supplemental new drug application (or any successor form(s) or application(s) having substantially the same effect with respect to the approval of a drug for marketing and sale) by the FDA with respect to one or more Products for the uUTI Indication and/or cUTI Indication (as applicable).

"**Form of Assignment and Transfer**" means the "Form of Assignment and Transfer" attached as Attachment 1 to the Form of Note attached hereto as Exhibit A.

"**Form of Note**" means the "Form of Note" attached hereto as Exhibit A.

"**GAAP**" means U.S. generally accepted accounting principles as in effect from time to time.

"**Global Note**" shall have the meaning specified in Section 2.05(b).

"**Gross Revenue**" means, as to any Products, for any Payment Measuring Period, the gross amount invoiced to and recognized as revenue on account of U.S. sales of such Products in accordance with GAAP by the Parent Guarantor or its Subsidiaries with respect to the sale by the Parent Guarantor or its Subsidiaries or licensees or sublicensees of Products. For purposes of clarity, Gross Revenue shall not include amounts invoiced to and recognized as revenue on account of sales outside the U.S.

Notwithstanding the foregoing, in the event that a Product is sold in the U.S. together with one or more other therapeutically active ingredients or therapies not constituting the Product for a single price (regardless of their packaging) (a "**Combination Sale**"), the gross amount recognized as revenue by the Parent Guarantor or its Subsidiaries on account of such Combination Sale shall be determined as follows:

(i) Except as provided below, the gross amount recognized as revenue for a Combination Sale in the U.S. shall be calculated by multiplying the gross amount invoiced for the Combination Sale ("**Gross Combination Sale Amount**") by the fraction A/(A+B), where A is the wholesale acquisition cost charged by the Parent Guarantor or its Subsidiaries or any of their respective licensees (collectively, "**Sellers**") if such Product is sold separately in the U.S. by any of the Sellers, and B is the wholesale acquisition cost charged by the Sellers for the other product(s) or active ingredients/components included in the Combination Sale if such other product(s) or active ingredients/components are sold separately by the Sellers in the U.S.

(ii) In the event that the Sellers sell the Product included in a Combination Sale as a separate product in the U.S., but do not separately sell all of the other product(s) or active ingredients/components, as the case may be, included in such Combination Sale in the U.S., the calculation of the gross amount recognized as revenue resulting from such Combination Sale shall be determined by multiplying the Gross Combination Sale Amount by the fraction A/C where A is the wholesale acquisition cost charged by the Sellers for such Product sold separately in the U.S., and C is the wholesale acquisition cost charged by the Sellers in the U.S. for such Combination Product.

(iii) In the event that the Sellers do not sell the Product included in a Combination Sale as a separate product in the U.S., but do separately sell all of the other products or active ingredients/components, as the case may be, included in the Combination Sale the U.S., the calculation of the gross amount recognized as revenue resulting from such Combination Sale shall be determined by multiplying the Gross Combination Sale Amount by the fraction (C-D)/C, where C is the wholesale acquisition cost charged by the Sellers for such Combination Product sold separately in the U.S., and D is the aggregate of the wholesale acquisition cost charged by the Sellers in the U.S., as applicable, of such other product(s) or active ingredients/components, as the case may be, included in the Combination Product and sold separately in the U.S.

If the calculation of the gross amount recognized as revenue on account of such Combination Sale resulting from a Combination Sale in the U.S. cannot be determined by any of the foregoing methods, the calculation of the revenue from such Combination Sale shall be calculated in a manner determined by the Parent Guarantor in good faith based upon the relative objective value of the active components of such Combination Product, in a manner consistent with GAAP.

"**Guarantee**" means the guarantee of the Company's obligations under this Indenture and the Notes, issued by the Guarantors pursuant to Article 13 of this Indenture.

"**Guarantee Obligations**" shall have the meaning specified in Section 13.01(a).

"**Guarantor Senior Debt**" means all obligations of any Guarantor to Silicon Valley Bank now existing or hereafter arising, including, without limitation, (i) the Obligations (as defined in the SVB Facility), together with all costs of collecting such obligations (including attorneys' fees), (ii) all obligations now existing or hereafter arising under any agreement in connection with the provision by Silicon Valley Bank to any Guarantor of products and/or credit services facilities, including, without limitation, any letters of credit, cash management services (including, without limitation, merchant services, direct deposit of payroll, business credit cards, and check cashing services), interest rate swap arrangements, and foreign exchange services, (iii) all interest accruing after the commencement by or against any Guarantor of any bankruptcy, reorganization or similar proceeding, whether or not a claim for post-petition interest is allowed as a claim in the proceeding and (iv) any obligations of the Guarantors hereafter arising that the applicable Guarantor(s) designate as "Guarantor Senior Debt"; provided, however, that the aggregate principal amount of any such indebtedness constituting Guarantor Senior Debt shall not exceed $50,000,000 outstanding at any time (it being understood that the maximum amount of Guarantor Senior Debt is not additive to the maximum amount of Senior Debt but instead refers to the same maximum amount as applied to each Guarantor with respect to Guarantor Senior Debt and to the Company with respect to Senior Debt).

"**Guarantors**" shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include their successors and assigns.

"**Holder**," as applied to any Note, or other similar terms (but excluding the term "beneficial holder"), means any Person in whose name at the time a particular Note is registered on the Note Register.

"**Holders' Representative**" means the Person named as the "Holders' Representative" in the first paragraph of this Indenture, until a successor Holders' Representative shall have become such pursuant to the applicable provisions of this Indenture, and thereafter "Holders' Representative" shall mean such successor Holders' Representative.

"**Holders' Representative Expenses**" shall have the meaning set forth in Section 9.08(b).

"**Holders' Representative Group**" shall have the meaning set forth in Section 9.08(b).

"**Indenture**" means this instrument as originally executed or, if amended or supplemented as herein provided, as so amended or supplemented.

"**Independent Accountant**" shall have the meaning set forth in Section 9.10(a).

"**Initial Purchasers**" means Advent Life Sciences LLP, Advent Life Sciences Fund II LP, Arix Bioscience Holdings Limited, Canaan X L.P., Frazier Healthcare VII, L.P., Frazier Healthcare VII-A, L.P., New Leaf Ventures III, L.P., New Leaf Biopharma Opportunities II, L.P., Sofinnova Venture Partners IX, L.P., Domain Partners IX, L.P., Pivotal bioVenture Partners Fund I, LP, Sarissa Capital Offshore Master Fund LP, Sarissa Capital Catapult Fund LLC, Sarissa Capital Hawkeye Fund LP, RA Capital Healthcare Fund, L.P., Blackwell Partners LLC – Series A, Empery Master Onshore, LLC, Empery Tax Efficient, LP, Empery Tax Efficient II, LP, Lincoln Park Capital Fund, LLC, 683 Capital Partners, LP, SilverArc Capital Alpha Fund I, L.P., SilverArc Capital Alpha Fund II, L.P., 2b LLC, Sabby Volatility Warrant Master Fund, Ltd., S.H.N Financial investments ltd, North Sound Trading, LP, CVI Investments, Inc., Salthill Investors (Bermuda) L.P., Salthill Partners, L.P. and Gary D. Cohn.

"**Interest Payment**" means, as to any Note, for each Payment Measuring Period, the Payment on such Note, but only to the extent that such Payment is described in clause (1) of the definition of Payment hereunder.

"**Investor Rights Agreement**" means the Investor Rights Agreement, dated as of January 21, 2020, among the Company and the Initial Purchasers.

"**Irish Guarantor** " shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns.

"**Iterum U.S. Holding** " shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns.

"**Iterum U.S. Limited** " shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns.

"**IV Product**" means the sulopenem antibiotic being developed by the Parent Guarantor for intravenous delivery.

"**Limited Recourse Net Revenues**" shall have the meaning specified in Section 2.03(b).

"**Limited Recourse Qualification**" shall have the meaning specified in Section 2.03(b).

"**Majority Holders**" means the Holders of Notes representing the right to receive no less than a majority of the Aggregate Principal Amount, on the terms and conditions set forth herein, determined as provided in Section 8.04.

"**Major Investors**" shall have the meaning set forth in the Investor Rights Agreement.

"**Maximum Return Amount**" means, as to any Note, the Maximum Return Amount set forth in such Note (which shall be 4,000 times the Principal Amount of such Note).

"**Maximum Return Amount Qualification**" means, as to any Note, the Maximum Return Amount Qualification set forth in such Note.

"**Minimum Principal Amount**" means $0.04.

"**Net Revenues**" means, as to any Products, for any Payment Measuring Period, the Gross Revenue in respect of such Products for such Payment Measuring Period, less the sum of the following to the extent attributable to activities in the U.S. that are incorporated in accordance with GAAP (except to the extent already excluded for Combination Sales in the definition of "Gross Revenue"): (a) customary sales returns actually made and allowances actually paid or taken, including trade, quantity and cash discounts, price adjustments, rebates, chargebacks, reimbursements or similar payments ordinarily granted or given but excluding discounts taken as part of bundling or other forms of multi-product purchase arrangements, (b) adjustments arising from consumer discount programs, (c) customs or excise duties, valued-added taxes, sales taxes, consumption taxes and other taxes (except income taxes) or duties relating to sales which are actually paid with respect to sales of Product, and (d) separately itemized freight and insurance incurred in shipping Product (to the extent that such costs are included in the amount invoiced to customers and included in Gross Revenue).

"**Note**" or "**Notes**" shall have the meaning specified in the first paragraph of the recitals of this Indenture.

"**Note Register**" shall have the meaning specified in Section 2.05(a).

"**Note Registrar**" shall have the meaning specified in Section 2.05(a).

"**Officer**" means, (i) with respect to the Company, the Company's President, Chief Executive Officer, Chief Financial Officer or Secretary or any director of the Company, (ii) with respect to the Parent Guarantor, the Parent Guarantor's President, Chief Executive Officer, Chief Financial Officer, Secretary, Treasurer or any director of the Parent Guarantor and (iii) with respect to any Subsidiary Guarantor, such Subsidiary Guarantor's President, Chief Executive Officer, Chief Financial Officer, Secretary or Treasurer, any director of such Subsidiary Guarantor, or any attorney appointed by such entity.

"**Officer's Certificate**," when used with respect to the Company or any Guarantor, means a certificate that is delivered to the Trustee and that is signed by an Officer of the Company or such Guarantor, as applicable. Each such certificate shall comply with Section 314 of the Trust Indenture Act and, except to the extent provided herein, shall include the statements provided for in Section 15.05 if and to the extent required by the provisions of such Section.

"**open of business**" means 9:00 a.m. (New York City time).

"**Opinion of Counsel**" means an opinion in writing signed by legal counsel, who may be an employee of or counsel to the Company, the Parent Guarantor or any of the Subsidiary Guarantors, as applicable, or other counsel that is acceptable to the Trustee, that is delivered to the Trustee, which opinion may contain customary exceptions and qualifications as to the matters set forth therein and which legal counsel may, in providing such opinion, rely upon certifications or other representations as to matters of fact. Each such opinion shall comply with Section 314 of the Trust Indenture Act and include the statements provided for in Section 15.05 if and to the extent required by the provisions of such Section 15.05.

"**Optional Redemption**" shall have the meaning specified in Section 14.01.

"**Oral Product**" means sulopenem etzadroxil and probenecid combined in a single bilayer tablet being developed by the Parent Guarantor for oral administration.

"**outstanding**," when used with reference to the Notes, shall, subject to the provisions of Section 8.04, mean, as of any particular time, all Notes authenticated and delivered by the Trustee under this Indenture, except:

(a) Notes theretofore canceled by the Trustee or accepted by the Trustee for cancellation;

(b) Notes, or portions thereof, that have become due and payable and in respect of which monies in the necessary amount shall have been deposited in trust with the Trustee or with any Paying Agent (other than the Company) or shall have been set aside and segregated in trust by the Company (if the Company shall act as its own Paying Agent);

(c) Notes that have been paid pursuant to Section 2.08 or Notes in lieu of which, or in substitution for which, other Notes shall have been authenticated and delivered pursuant to the terms of Section 2.06 unless proof satisfactory to the Trustee is presented that any such Notes are held by protected purchasers in due course; and

(d) Notes repurchased by the Company or the Guarantors pursuant to the penultimate sentence of Section 2.10.

"**Parent Guarantor**" shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns.

"**Paying Agent**" shall have the meaning specified in Section 4.02.

"**Payment**" means, as to any Note, for each Payment Measuring Period, any positive amount equal to the Pro Rata Share of such Note multiplied by the product of (a) the Net Revenues for such Payment Measuring Period, and (b) the applicable Payment Rate for such applicable Payment Measuring Period, subject to the End Date and the Maximum Return

Amount Qualification; provided that each Payment on such Note shall be (1) an Interest Payment on such Note, to the extent that the amount of such Payment, when added to the amounts of all prior Payments on such Note, sums to an amount that is less than or equal to the difference of (x) the Maximum Return Amount for such Note less (y) the Principal Amount of such Note (such difference being the "**Maximum Interest Payment Amount**"), and (2) a Principal Payment on such Note, to the extent that the amount of such Payment, when added to the amounts of all prior Payments on such Note, sums to an amount greater than the Maximum Interest Payment Amount.

"**Payment Date**" means any date on which a Payment is made by the Company to the Depositary in accordance with Section 2.03(b).

"**Payment Measuring Period**" means a period equal to the prior six (6) months, calculated as of June 30 and December 31 of each calendar year during the term of this Indenture; provided no Payment Measuring Period shall commence after the End Date.

"**Payment Rate** " means, for each Payment Measuring Period, as measured at the end of such Payment Measuring Period: (a) for any Payment Measuring Period in which the Parent Guarantor (or Affiliate thereof) receives, or has previously received, FDA Approval for the uUTI Indication, a percentage equal to the uUTI Payment Rate multiplied by a number equal to the Aggregate Principal Amount; or (b) for any Payment Measuring Period in which the Parent Guarantor (or Affiliate thereof) receives, or has previously received, FDA Approval for the cUTI Indication, but has not received FDA Approval for the uUTI Indication, a percentage equal to the cUTI Indication Payment Rate multiplied by a number equal to the Aggregate Principal Amount.

"**Payment Record Date**," with respect to any Payment Date, means the fifteenth (15th) day (whether or not such day is a Business Day) immediately preceding the applicable Payment Date.

"**Payment Statement**" means, with respect to each Payment Measuring Period occurring prior to the End Date, the written statement of the Company and the Parent Guarantor (together with a certification and acknowledgment that no events of default under the Senior Debt owing to Silicon Valley Bank have occurred and are continuing or would result from any Payments from the Company reflected in the Payment Statement, which certification shall also be acknowledged in writing by Silicon Valley Bank, and any of its successors and assigns, for so long as its Senior Debt is outstanding), certified by the Chief Financial Officer of the Parent Guarantor and an authorized officer of the Company, setting forth with reasonable detail:

(a) for each Product:

(i) (x) the total of the invoice price charged by the Parent Guarantor, its Affiliates and its licensees for sales of the Product by the Parent Guarantor, its Affiliates and licensees to third parties during the applicable Payment Measuring Period, (y) calculations of Gross Revenue and Net Revenues during the applicable Payment

Measuring Period, (z) the applicable Payment Rate for the applicable Payment Measuring Period and (aa) the allocation of any payment for the applicable Payment Measuring Period as between Principal Payment and Interest Payment portions thereof; and

(ii) to the extent that Gross Revenue for the Product during the applicable Payment Measuring Period is determined based on a Combination Product, the method of determining the Gross Revenue and Net Revenues of the Combination Product attributable to the Product in accordance with the definitions of Gross Revenue and Net Revenues;

(b) the amount of any Default Interest accruing during such Payment Measuring Period; and

(c) notice of whether any FDA Approval has been granted during the applicable Payment Measuring Period.

The amounts in the Payment Statement shall be calculated in accordance with the Accounting Standards and shall be derived from and consistent with the audited financial statements contained in the reports filed with the Trustee pursuant to Section 5.04(b) of this Indenture.

"**Permitted Denomination**" means having a Principal Amount in any increment of the Minimum Principal Amount.

"**Person**" means an individual, a corporation, a company, a limited liability company, an association, a partnership, a joint venture, a joint stock company, a trust, an unincorporated organization or a government or an agency or a political subdivision thereof.

"**PFIC**" shall have the meaning specified in Section 4.10(b).

"**Pfizer License**" means that License Agreement, by and among the Parent Guarantor, the Irish Guarantor and Pfizer Inc., dated as of November 18, 2015, as it may be amended or otherwise modified from time to time.

"**Physical Notes**" means permanent certificated Notes in registered form issued in a Permitted Denomination.

"**Predecessor Note**" of any particular Note means every previous Note evidencing all or a portion of the same debt as that evidenced by such particular Note; and, for the purposes of this definition, any Note authenticated and delivered under Section 2.06 in lieu of or in exchange for a mutilated, lost, destroyed or stolen Note shall be deemed to evidence the same debt as the mutilated, lost, destroyed or stolen Note that it replaces.

"**Principal Amount**" means, for any Note, the Principal Amount set forth in such Note (which shall be a Permitted Denomination).

"**Principal Amount Multiple**" means for any Note, the product of the Principal Amount and 100.

"**Principal Payment**" means, as to any Note, for each Payment Measuring Period, the Payment on such Note, but only to the extent that such Payment is described in clause (2) of the definition of Payment hereunder.

"**Pro Rata Share**" means, as to any Note, a fraction, the numerator of which is the Principal Amount for such Note, and the denominator of which is the Aggregate Principal Amount.

"**Products**" means the Oral Product and the IV Product and "Product" means any one of them.

"**Redemption Date**" shall have the meaning specified in Section 14.02(a).

"**Redemption Notice**" shall have the meaning specified in Section 14.02(a).

"**Redemption Price**" shall have the meaning specified in Section 14.01.

"**Representative Expense Fund**" shall have the meaning specified in Section 9.08(b).

"**Representatives**" shall have the meaning specified in Section 4.12.

"**Resale Restriction Termination Date**" shall have the meaning specified in Section 2.05(c).

"**Responsible Officer**" means, when used with respect to the Trustee, any officer within the corporate trust department of the Trustee, having direct responsibility for the administration of this Indenture or any other officer of the Trustee to whom any corporate trust matter is referred because of such person's knowledge of and familiarity with the particular subject.

"**Restricted Actions**" shall have the meaning set forth in Section 4.11.

"**Restricted Securities**" shall have the meaning specified in Section 2.05(c).

"**Rights Offering**" means any public offering of subscription rights to purchase units consisting of Notes and Exchangeable Senior Subordinated Notes by the Parent Guarantor and the Company to holders, at the date of this Indenture, of ordinary shares of the Parent Guarantor, nominal value $0.01 per share on a pro rata basis in accordance with their share ownership as of a record date to be determined by the Board of Directors of the Parent Guarantor or a committee thereof. The Initial Purchasers and their Affiliates shall not be entitled to purchase any units pursuant to the Rights Offering (regardless of whether or not under Irish or other applicable law such subscription rights are required to be offered to the Initial Purchasers).

"**Rule 144**" means Rule 144 as promulgated under the Securities Act.

"**Rule 144A**" means Rule 144A as promulgated under the Securities Act.

"**Securities Act**" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"**Senior Debt** " means all obligations of the Company to Silicon Valley Bank now existing or hereafter arising, including, without limitation, (i) the Obligations (as defined in the SVB Facility), together with all costs of collecting such obligations (including attorneys' fees), (ii) all obligations now existing or hereafter arising under any agreement in connection with the provision by Silicon Valley Bank to the Company of products and/or credit services facilities, including, without limitation, any letters of credit, cash management services (including, without limitation, merchant services, direct deposit of payroll, business credit cards, and check cashing services), interest rate swap arrangements, and foreign exchange services, (iii) all interest accruing after the commencement by or against the Company of any bankruptcy, reorganization or similar proceeding, whether or not a claim for post-petition interest is allowed as a claim in the proceeding and (iv) any obligations of the Company hereafter arising that the Parent Guarantor designates as "Senior Debt"; provided, however, that the aggregate principal amount of any such indebtedness shall not exceed $50,000,000 outstanding at any time (it being understood that the maximum amount of Senior Debt is not additive to the maximum amount of Guarantor Senior Debt but instead refers to the same maximum amount as applied to the Company with respect to Senior Debt and to each Guarantor with respect to Guarantor Senior Debt).

"**Significant Subsidiary**" means a Subsidiary of the Parent Guarantor that meets the definition of "significant subsidiary" in Article 1, Rule 1-02 of Regulation S-X under the Exchange Act.

"**Subsidiary**" means, with respect to any Person, any corporation, association, partnership or other business entity of which more than 50% of the total voting power of shares of Capital Stock or other interests (including partnership interests) entitled (without regard to the occurrence of any contingency) to vote in the election of directors, managers, general partners or trustees thereof is at the time owned or controlled, directly or indirectly, by (i) such Person; (ii) such Person and one or more Subsidiaries of such Person; or (iii) one or more Subsidiaries of such Person.

"**Subsidiary Guarantors**" shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns.

"**Successor Company**" shall have the meaning specified in Section 11.01(a).

"**SVB Facility**" means that certain Loan and Security Agreement among the Subsidiary Guarantors, the Company and Silicon Valley Bank dated as of April 27, 2018 (as may be

amended, modified, restated, replaced, or supplemented from time to time, including any deferrals, renewals, refinancings or extensions thereof).

"**transfer**" shall have the meaning specified in Section 2.05(c).

"**Treasury Regulations**" shall have the meaning specified in Section 4.10(c).

"**Trust Indenture Act**" means the U.S. Trust Indenture Act of 1939, as amended, as it was in force at the date of execution of this Indenture; *provided*, *however*, that in the event the Trust Indenture Act of 1939 is amended after the date hereof, the term "Trust Indenture Act" shall mean, to the extent required by such amendment, the Trust Indenture Act of 1939, as so amended.

"**Trustee**" means the Person named as the "**Trustee**" in the first paragraph of this Indenture until a successor trustee shall have become such pursuant to the applicable provisions of this Indenture, and thereafter "**Trustee**" shall mean or include each Person who is then a Trustee hereunder.

"**Uncurable Event of Default**" has the meaning set forth in Section 2.03(d)(ii).

"**uUTI Indication**" means the uncomplicated urinary tract infection indication.

"**uUTI Payment Rate**" means 0.00015%; provided, that if the aggregate Principal Amounts in respect of all Notes issued and outstanding immediately after completion of the Rights Offering exceeds $100,000, the uUTI Indication Payment Rate means 0.00015% multiplied by a fraction, the numerator of which is $100,000, and the denominator of which is the aggregate Principal Amounts in respect of all Notes issued and outstanding immediately after completion of the Rights Offering.

"**Veto Notice**" shall have the meaning set forth in Section 4.11.

Section 1.02. *Tax Treatment*. The Company agrees and, by acceptance of a Note, each beneficial owner of a Note will be deemed to have agreed (i) to treat the Notes for U.S. federal income tax purposes as a contractual right to receive Payments from the Company as and when such Payments become payable pursuant to the terms of the Notes and not as indebtedness of, or equity in, the Company or any other Person for U.S. federal income tax purposes and (ii) to be bound (in the absence of an administrative determination or judicial ruling to the contrary) by such treatment for U.S. federal income tax purposes. The parties to this Indenture do not intend to create a partnership for any purpose, and no party to this Indenture nor any beneficial owner of a Note shall be treated as a partner for any purpose.

Section 1.03. *References to Interest.* Notwithstanding the references herein to Interest Payments, Default Interest, and similar terms, for the avoidance of doubt, no interest shall accrue on any Principal Amount of any Note other than (a) Default Interest accruing on any Principal Amount that is a Defaulted Amount pursuant to Section 2.03(d)(i), and (b) Default Interest

accruing pursuant to Section 2.03(d)(ii), and all other interest in respect of the Notes shall accrue and be payable only to the extent that such interest is an Interest Payment.

ARTICLE 2
ISSUE, DESCRIPTION, EXECUTION, REGISTRATION AND EXCHANGE OF NOTES

Section 2.01. *Designation and Amount.* The Notes shall be designated as the "Limited Recourse Royalty-Linked Subordinated Notes." The aggregate Principal Amounts of Notes that may be authenticated and delivered under this Indenture is limited to $120,000, except for Notes authenticated and delivered upon registration or transfer of, or in exchange for, or in lieu of other Notes pursuant to Section 2.05, Section 2.06, Section 2.07, and Section 10.04.

Section 2.02. *Form of Notes.* The Notes and the Trustee's certificate of authentication to be borne by such Notes shall be substantially in the respective forms set forth in Exhibit A, the terms and provisions of which shall constitute, and are hereby expressly incorporated in and made a part of this Indenture. To the extent applicable, the Company, the Guarantors and the Trustee, by their execution and delivery of this Indenture, expressly agree to such terms and provisions and to be bound thereby.

Any Global Note may be endorsed with or have incorporated in the text thereof such legends or recitals or changes not inconsistent with the provisions of this Indenture as may be required by the Custodian or the Depositary, or as may be required to comply with any applicable law or any regulation thereunder or with the rules and regulations of any securities exchange or automated quotation system upon which the Notes may be listed or traded or designated for issuance or to conform with any usage with respect thereto, or to indicate any special limitations or restrictions to which any particular Notes are subject.

Any of the Notes may have such letters, numbers or other marks of identification and such notations, legends or endorsements as the Officers executing the same may approve (execution thereof to be conclusive evidence of such approval) and as are not inconsistent with the provisions of this Indenture, or as may be required to comply with any law or with any rule or regulation made pursuant thereto or with any rule or regulation of any securities exchange or automated quotation system on which the Notes may be listed or designated for issuance, or to conform to usage or to indicate any special limitations or restrictions to which any particular Notes are subject.

Each Global Note shall provide that it shall represent outstanding Notes representing the aggregate Principal Amounts from time to time endorsed thereon and that the aggregate Principal Amounts of outstanding Notes represented thereby may from time to time be increased or reduced to reflect repurchases, cancellations, transfers or exchanges permitted hereby. Any endorsement of a Global Note to reflect the amount of any increase or decrease in the aggregate Principal Amounts of outstanding Notes represented thereby shall be made by the Trustee or the Custodian, at the direction of the Trustee, in such manner and upon instructions given by the Company or the Holder of such Notes in accordance with this Indenture. Payment of Principal

Payments and Interest Payments for, and any accrued and unpaid Default Interest on, a Global Note shall be made to the Holder of such Note on the date of payment, unless a record date or other means of determining Holders eligible to receive payment is provided for herein.

Section 2.03. *Denomination of Notes; Payments on Notes, Default Interest and Defaulted Amounts*.

(a) The Notes shall be issuable in registered form without coupons in any Permitted Denomination.

(b) Subject to Section 11.04 , beginning with the Payment Measuring Period ending on June 30, 2020, and for each following Payment Measuring Period until the Payment Measuring Period ending on the End Date, within 75 days of the end of the applicable Payment Measuring Period, subject to the Aggregate Maximum Return Amount Qualification, the Company shall (i) provide notice to the Holders' Representative of any Payments due and payable in respect of the Notes and (ii) pay such Payments to each Depositary or its respective nominee, as the case may be, as the registered Holders of the Notes, in immediately available funds in lawful money of the United States; provided that (A) no Payments, Designated Default Interest or respective portions thereof shall be payable by the Company in respect of any period after the End Date, (B) no Payment, Designated Default Interest or respective portion thereof shall be payable by the Company to the extent that the Company has paid, or through payment of such Payments or Designated Default Interest will have paid, in excess of an aggregate sum of Payments and Designated Default Interest on account of the Notes equal to the Aggregate Maximum Return Amount (this clause (B) being referred to as the "**Aggregate Maximum Return Amount Qualification**") and (C) each Interest Payment in respect of the Notes shall be based solely on Net Revenues earned on U.S. sales of the Products in the applicable Payment Measuring Period, if any (the "**Limited Recourse Net Revenues**"), and in no event shall the Company be obligated to make any Interest Payment in respect of the Notes on account of any assets or properties other than the Limited Recourse Net Revenues (this clause (C) being referred to as the "**Limited Recourse Qualification**").

The Notes will be subject to optional redemption by the Company as set forth in Article 14 of this Indenture.

For the avoidance of doubt, (a) once Payments and Designated Default Interest in an aggregate amount equal to the Aggregate Maximum Return Amount has been paid in respect of the Notes (whether pursuant to the Notes, pursuant to Article 14 of this Indenture, or otherwise), no further Payments or Designated Default Interest shall be payable on the Notes, and no further Default Interest shall accrue pursuant to Section 2.03(d), (b) if and to the extent that Limited Recourse Net Revenues have not been generated (other than as a result of a breach of Section 4.14), no amounts other than Principal Payments shall be payable on the Notes, (c) if any portion of the Principal Amount in respect of any Note has not been paid as of the End Date, the Company shall pay such unpaid portion of the Principal Amount to the holder thereof

notwithstanding the Limited Recourse Qualification and (d) in no event will Pfizer Inc. have any obligations to any Holder pursuant to this Indenture or the Notes.

(c) The Person in whose name any Note (or its Predecessor Note) is registered on the Note Register at the close of business on any Payment Record Date with respect to any Payment Date shall be entitled to receive the Payment and Default Interest, if any, payable on such Payment Date. The Payment and Default Interest, if any, with respect to any Note (i) in the case of any Physical Note, shall be payable at the office or agency of the Company maintained by the Company for such purposes in the United States of America, which shall initially be the office of the Trustee located in the United States of America, or any other office or agency located in the United States of America so designated by the Trustee and (ii) in the case of any Global Note, shall be payable by wire transfer of immediately available funds to the account of the Depositary or its nominee.

(d) Any interest set forth in subsection (i) and (ii) below shall be referred to herein as "Default Interest."

(i) Any Defaulted Amounts shall forthwith cease to be payable to the Holder on the relevant payment date but shall accrue Default Interest, to the extent permitted by applicable law, at the Default Rate, from, and including, such relevant payment date, and such Defaulted Amounts together with any such Default Interest thereon shall be paid by the Company, at its election in each case, as provided in clause (A) or (B) below:

(A) The Company may elect to make payment of any Defaulted Amounts and Default Interest thereon to the Persons in whose names the Notes (or their respective Predecessor Notes) are registered at the close of business on a special record date for the payment of such Defaulted Amounts and Default Interest, which shall be fixed in the following manner. The Company shall notify the Trustee in writing of the amount of the Defaulted Amounts and Default Interest proposed to be paid on each Note and the date of the proposed payment (which shall be not less than 25 days after the receipt by the Trustee of such notice, unless the Trustee shall consent to an earlier date), and at the same time the Company shall deposit with the Trustee an amount of money equal to the aggregate amount to be paid in respect of such Defaulted Amounts and Default Interest or shall make arrangements satisfactory to the Trustee for such deposit on or prior to the date of the proposed payment, such money when deposited to be held in trust for the benefit of the Persons entitled to such Defaulted Amounts and Default Interest as in this clause provided. Thereupon the Company shall fix a special record date for the payment of such Defaulted Amounts and Default Interest which shall be not more than 15 days and not less than 10 days prior to the date of the proposed payment, and not less than 10 days after the receipt by the Trustee of the notice of the proposed payment. The Company shall promptly notify the Trustee in writing of such special record date and the Trustee, in the name and at the expense of the Company, shall cause notice of the proposed

payment of such Defaulted Amounts and Default Interest and the special record date therefor to be delivered to each Holder at its address as it appears in the Note Register, or by electronic means to the Depositary in the case of Global Notes, not less than 10 days prior to such special record date. Notice of the proposed payment of such Defaulted Amounts and Default Interest and the special record date therefor having been so delivered, such Defaulted Amounts and Default Interest shall be paid to the Persons in whose names the Notes (or their respective Predecessor Notes) are registered at the close of business on such special record date and shall no longer be payable pursuant to the following clause (B) of this Section 2.03(d)(i).

(B) The Company may make payment of any Defaulted Amounts and Default Interest in any other lawful manner not inconsistent with the requirements of any securities exchange or automated quotation system on which the Notes may be listed or designated for issuance, and upon such notice as may be required by such exchange or automated quotation system, if, after written notice given by the Company to the Trustee of the proposed payment pursuant to this clause, such manner of payment shall be deemed practicable by the Trustee.

(ii) Default Interest shall accrue, with respect to each Note, on the Principal Amount Multiple of such Note, on a per diem basis, from and after the occurrence of, and during the continuance of, any Event of Default pursuant to paragraphs (b), (c), and (f) of Section 6.01 and through and including the earlier of the End Date and the date that Payments and Designated Default Interest in an aggregate amount equal to the Aggregate Maximum Return Amount have been paid in respect of the Notes (whether pursuant to the Notes, pursuant to Article 14 of this Indenture, or otherwise), provided, that in the case of any Event of Default that has occurred pursuant to paragraphs (c) or (f) of Section 6.01 and is not by its nature subject to termination or cure (an "**Uncurable Event of Default**"), such Default Interest shall constitute Designated Default Interest. Such Default Interest shall become due and payable on the first Payment Date to occur after the occurrence of such Event of Default, and on each Payment Date thereafter that corresponds to any Payment Measuring Period during which such Event of Default shall be continuing. Such Default Interest shall not be deemed to constitute liquidated damages and shall be in addition to, and not in lieu of, any other remedies (including nonmonetary injunctive and declaratory relief and any action for damages) that the Holders shall be entitled to seek as a result of the occurrence of any Event of Default pursuant to paragraphs (b), (c), and (f) of Section 6.01; provided, that the Holders shall have no right to accelerate payment of any amount in respect of the Notes. The Company and the Guarantors irrevocably waive any right to claim that Default Interest is the exclusive remedy of the Holders or Holders' Representative arising from any such Event of Default.

Section 2.04. *Execution, Authentication and Delivery of Notes.* The Notes shall be signed in the name and on behalf of the Company by the manual or facsimile signature of an Officer of the Company.

At any time and from time to time after the execution and delivery of this Indenture, the Company may deliver Notes executed by the Company to the Trustee for authentication, together with a Company Order for the authentication and delivery of such Notes, and the Trustee in accordance with such Company Order shall authenticate and deliver such Notes, without any further action by the Company hereunder, other than delivery of an Officer's Certificate pursuant to Section 15.05. For the avoidance of doubt, the Trustee shall not be obligated to authenticate a Note hereunder unless and until it has received a Company Order in accordance with the terms hereof.

Only such Notes as shall bear thereon a certificate of authentication substantially in the form set forth on the form of Note attached as Exhibit A hereto, executed manually by an authorized signatory of the Trustee (or an authenticating agent appointed by the Trustee as provided by Section 15.10), shall be entitled to the benefits of this Indenture or be valid or obligatory for any purpose. Such certificate by the Trustee (or such an authenticating agent) upon any Note executed by the Company shall be conclusive evidence that the Note so authenticated has been duly authenticated and delivered hereunder and that the Holder is entitled to the benefits of this Indenture.

In case any Officer of the Company who shall have signed any of the Notes shall cease to be such Officer before the Notes so signed shall have been authenticated and delivered by the Trustee, or disposed of by the Company, such Notes nevertheless may be authenticated and delivered or disposed of as though the Person who signed such Notes had not ceased to be such Officer of the Company; and any Note may be signed on behalf of the Company by such persons as, at the actual date of the execution of such Note, shall be the Officers of the Company, although at the date of the execution of this Indenture any such Person was not such an Officer.

Section 2.05. *Exchange and Registration of Transfer of Notes; Restrictions on Transfer; Depositary.*

(a) The Company shall cause to be kept at the Corporate Trust Office a register (the register maintained in such office or in any other office or agency of the Company designated pursuant to Section 4.02, the "**Note Register**") in which, subject to such reasonable regulations as it may prescribe, the Company shall provide for the registration of Notes and of transfers of Notes. Such register shall be in written form or in any form capable of being converted into written form within a reasonable period of time. The Trustee is hereby initially appointed the "**Note Registrar**" for the purpose of registering Notes and transfers of Notes as herein provided. The Company may appoint one or more co-Note Registrars in accordance with Section 4.02.

Upon surrender for registration of transfer of any Note to the Note Registrar or any co-Note Registrar, and satisfaction of the requirements for such transfer set forth in this Section

2.05, the Company shall execute, and upon receipt of a Company Order, the Trustee shall authenticate and deliver, in the name of the designated transferee or transferees, one or more new Notes of any Permitted Denominations and of a like Permitted Denomination in the aggregate, and bearing such restrictive legends as may be required by this Indenture.

Notes may be exchanged for other Notes of any Permitted Denominations and of a like Permitted Denomination in the aggregate, upon surrender of the Notes to be exchanged at any such office or agency maintained by the Company pursuant to Section 4.02. Whenever any Notes are so surrendered for exchange, the Company shall execute, and upon receipt of a Company Order, the Trustee shall authenticate and deliver, the Notes that the Holder making the exchange is entitled to receive, bearing registration numbers not contemporaneously outstanding.

All Notes presented or surrendered for registration of transfer or for exchange or repurchase shall (if so required by the Company, the Trustee, the Note Registrar or any co-Note Registrar) be duly endorsed, or be accompanied by a written instrument or instruments of transfer in form satisfactory to the Note Registrar and the Company and duly executed, by the Holder thereof or its attorney-in-fact duly authorized in writing.

No service charge shall be imposed by the Company, the Trustee, the Note Registrar, any co-Note Registrar or the Paying Agent for any exchange or registration of transfer of Notes, but the Trustee, the Note Registrar or the Company may require a Holder to pay a sum sufficient to cover any documentary, stamp or similar issue or transfer tax required in connection therewith as a result of the name of the Holder of new Notes issued upon such exchange or registration of transfer being different from the name of the Holder of the old Notes surrendered for exchange or registration of transfer.

All Notes issued upon any registration of transfer or exchange of Notes in accordance with this Indenture shall be the valid obligations of the Company, evidencing the same debt, and entitled to the same benefits under this Indenture as the Notes surrendered upon such registration of transfer or exchange.

(b) The initial Notes issued hereunder on the date of this Indenture shall be represented by Physical Notes. Thereafter, so long as the Notes are eligible for book-entry settlement with the Depositary, unless otherwise required by law, subject to the fourth paragraph from the end of Section 2.05(c) all Notes shall be represented by one or more Notes in global form (each, a "**Global Note**") registered in the name of the Depositary or the nominee of the Depositary. The transfer and exchange of beneficial interests in a Global Note that does not involve the issuance of a Physical Note shall be effected through the Depositary (but not the Trustee or the Custodian) in accordance with this Indenture (including the restrictions on transfer set forth herein) and the procedures of the Depositary therefor.

(c) Every Note that bears or is required under this Section 2.05(c) to bear the legend set forth in this Section 2.05(c) (the "**Restricted Securities**") shall be subject to the restrictions on transfer set forth in this Section 2.05(c) (including those contained in the legend set forth

below), unless such restrictions on transfer shall be eliminated or otherwise waived by written consent of the Company, and the Holder of each such Restricted Security, by such Holder's acceptance thereof, agrees to be bound by all such restrictions on transfer. As used in this Section 2.05(c), the term "**transfer**" encompasses any sale, pledge, transfer or other disposition whatsoever of any Restricted Security. For the avoidance of doubt, nothing in this Section 2.05(c) shall be deemed to prevent the transfer of any Note by any Holder to any Affiliate of such Holder in a transaction that is otherwise in compliance with the Securities Act.

Until the date (the "**Resale Restriction Termination Date**") that is the later of (1) the date that is one year after the last date of original issuance of the Notes, or such shorter period of time as permitted by Rule 144 or any successor provision thereto, and (2) such later date, if any, as may be required by applicable law, including as a result of the affiliate status of any holder of a Note, any certificate evidencing such Note (and all securities issued in exchange therefor or substitution thereof shall bear a legend in substantially the following form (unless such Notes have been transferred pursuant to a registration statement that has become or been declared effective under the Securities Act and that was effective at the time of such transfer, or sold pursuant to the exemption from registration provided by Rule 144 or any similar provision then in force under the Securities Act, or unless otherwise agreed by the Company in writing, with notice thereof to the Trustee):

THIS SECURITY HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "**SECURITIES ACT**"), AND MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED EXCEPT IN ACCORDANCE WITH THE FOLLOWING SENTENCE. BY ITS ACQUISITION HEREOF OR OF A BENEFICIAL INTEREST HEREIN, THE ACQUIRER:

(i) REPRESENTS THAT IT AND ANY ACCOUNT FOR WHICH IT IS ACTING IS AN "ACCREDITED INVESTOR" (WITHIN THE MEANING OF RULE 501 UNDER THE SECURITIES ACT) AND THAT IT EXERCISES SOLE INVESTMENT DISCRETION WITH RESPECT TO EACH SUCH ACCOUNT, AND THAT IT AND ANY SUCH ACCOUNT IS NOT AN AFFILIATE OF ITERUM THERAPEUTICS BERMUDA LIMITED (THE "**COMPANY**"), ITERUM THERAPEUTICS PLC (THE "**PARENT GUARANTOR**"), ITERUM THERAPEUTICS INTERNATIONAL LIMITED (THE "**IRISH GUARANTOR**"), ITERUM THERAPEUTICS US LIMITED ("**ITERUM U.S. LIMITED**") OR ITERUM THERAPEUTICS US HOLDING LIMITED (TOGETHER WITH THE PARENT GUARANTOR, THE IRISH GUARANTOR AND ITERUM U.S. LIMITED, THE "**GUARANTORS**"), AND

(ii) AGREES FOR THE BENEFIT OF THE COMPANY AND THE GUARANTORS THAT IT WILL NOT OFFER, SELL, PLEDGE OR OTHERWISE TRANSFER THIS SECURITY OR ANY BENEFICIAL INTEREST HEREIN PRIOR TO THE DATE THAT IS THE LATER OF (X) ONE YEAR AFTER THE LAST ORIGINAL ISSUE DATE HEREOF OR SUCH SHORTER PERIOD OF TIME AS

PERMITTED BY RULE 144 UNDER THE SECURITIES ACT OR ANY SUCCESSOR PROVISION THERETO AND (Y) SUCH LATER DATE, IF ANY, AS MAY BE REQUIRED BY APPLICABLE LAW, EXCEPT:

(A) TO THE PARENT GUARANTOR OR ANY SUBSIDIARY THEREOF (INCLUDING THE COMPANY), OR

(B) PURSUANT TO A REGISTRATION STATEMENT WHICH HAS BECOME EFFECTIVE UNDER THE SECURITIES ACT, OR

(C) TO A QUALIFIED INSTITUTIONAL BUYER IN COMPLIANCE WITH RULE 144A UNDER THE SECURITIES ACT, OR

(D) PURSUANT TO AN EXEMPTION FROM REGISTRATION PROVIDED BY RULE 144 UNDER THE SECURITIES ACT OR ANY OTHER AVAILABLE EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

PRIOR TO THE REGISTRATION OF ANY TRANSFER IN ACCORDANCE WITH CLAUSE (2)(D) ABOVE, THE COMPANY, THE GUARANTORS AND THE TRUSTEE RESERVE THE RIGHT TO REQUIRE THE DELIVERY OF SUCH LEGAL OPINIONS, CERTIFICATIONS OR OTHER EVIDENCE AS MAY REASONABLY BE REQUIRED IN ORDER TO DETERMINE THAT THE PROPOSED TRANSFER IS BEING MADE IN COMPLIANCE WITH THE SECURITIES ACT AND APPLICABLE STATE SECURITIES LAWS. NO REPRESENTATION IS MADE AS TO THE AVAILABILITY OF ANY EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

THE HOLDER OF THIS SECURITY IS ENTITLED TO THE BENEFITS OF AN INVESTOR RIGHTS AGREEMENT (AS SUCH TERM IS DEFINED IN THE INDENTURE REFERRED TO ON THE REVERSE HEREOF) AND, BY ITS ACCEPTANCE HEREOF, AGREES TO BE BOUND BY AND TO COMPLY WITH THE PROVISIONS OF SUCH INVESTOR RIGHTS AGREEMENT.

No transfer prior to the Resale Restriction Termination Date of any Note as to which such restrictions on transfer apply will be registered by the Note Registrar unless the applicable box on the Form of Assignment and Transfer has been checked.

Any Note (or security issued in exchange or substitution therefor) as to which such restrictions on transfer shall have expired in accordance with their terms may, upon surrender of such Note for exchange to the Note Registrar in accordance with the provisions of this Section 2.05, be exchanged for a new Note or Notes, of like Permitted Denomination in the aggregate, which shall not bear the restrictive legend required by this Section 2.05(c) and shall not be assigned a restricted CUSIP number. The Company shall be entitled to instruct the Custodian in writing to so surrender any Global Note as to which such restrictions on transfer shall have

expired in accordance with their terms for exchange, and, upon such instruction, the Custodian shall so surrender such Global Note for exchange; and any new Global Note so exchanged therefor shall not bear the restrictive legend specified in this Section 2.05(c) and shall not be assigned a restricted CUSIP number. The Company shall promptly notify the Trustee in writing upon the occurrence of the Resale Restriction Termination Date and promptly after a registration statement, if any, with respect to the Notes has been declared effective under the Securities Act.

Notwithstanding any other provisions of this Indenture (other than the provisions set forth in this Section 2.05(c)), a Global Note may not be transferred as a whole or in part except (i) by the Depositary to a nominee of the Depositary or by a nominee of the Depositary to the Depositary or another nominee of the Depositary or by the Depositary or any such nominee to a successor Depositary or a nominee of such successor Depositary and (ii) for transfers of portions of a Global Note in certificated form made upon request of a member of, or a participant in, the Depositary (for itself or on behalf of a beneficial owner) by written notice given to the Trustee by or on behalf of the Depositary in accordance with customary procedures of the Depositary and in compliance with this Section 2.05(c).

The Depositary shall be a clearing agency registered under the Exchange Act. The Company initially appoints The Depository Trust Company to act as Depositary with respect to each Global Note. Initially, each Global Note shall be issued to the Depositary, registered in the name of Cede & Co., as the nominee of the Depositary, and deposited with the Trustee as custodian for Cede & Co.

Only if (i) the Depositary notifies the Company at any time that the Depositary is unwilling or unable to continue as depositary for the Global Notes and a successor depositary is not appointed within 90 days, (ii) the Depositary ceases to be registered as a clearing agency under the Exchange Act and a successor depositary is not appointed within 90 days, (iii) a beneficial owner of any Global Note notifies the Company that it is an Affiliate of the Company or the Parent Guarantor and requests that its beneficial interest therein be issued as a Physical Note, or (iv) an Event of Default with respect to the Notes has occurred and is continuing and a beneficial owner of any Global Note requests that its beneficial interest therein be issued as a Physical Note, the Company shall execute, and the Trustee, upon receipt of an Officer's Certificate and a Company Order for the authentication and delivery of Notes, shall authenticate and deliver at the Company's expense (x) in the case of clause (iii) or (iv), a Physical Note to such beneficial owner in a Permitted Denomination corresponding to such beneficial owner's beneficial interest in the related Global Note, and (y) in the case of clause (i) or (ii), Physical Notes to each beneficial owner of the related Global Notes (or a portion thereof), each in a Permitted Denomination corresponding to the applicable beneficial owner's beneficial interest in the related Global Note and collectively in an aggregate Permitted Denomination equal to the aggregate Permitted Denomination of such Global Notes in exchange for such Global Notes, and upon delivery of the Global Notes to the Trustee such Global Notes shall be canceled.

Physical Notes issued in exchange for all or a part of the Global Note pursuant to this Section 2.05(c) shall be registered in such names and in such Permitted Denominations as the

Depositary, pursuant to instructions from its direct or indirect participants or otherwise, or, in the case of clause (iii) or (iv) of the immediately preceding paragraph, the relevant beneficial owner, shall instruct the Trustee in writing. Upon execution and authentication, the Trustee shall deliver at the Company's expense such Physical Notes to the Persons in whose names such Physical Notes are so registered.

At such time as all interests in a Global Note have been canceled, repurchased, redeemed or transferred, such Global Note shall be, upon receipt thereof, canceled by the Trustee in accordance with standing procedures and existing instructions between the Depositary and the Custodian. At any time prior to such cancellation, if any interest in a Global Note is exchanged for Physical Notes, canceled or transferred to a transferee who receives Physical Notes therefor or any Physical Note is exchanged, redeemed, repurchased or transferred for part of such Global Note, the Permitted Denomination of such Global Note shall, in accordance with the standing procedures and instructions existing between the Depositary and the Custodian, be appropriately reduced or increased, as the case may be, and an endorsement shall be made on such Global Note, by the Trustee or the Custodian, at the direction of the Trustee, to reflect such reduction or increase.

None of the Company, the Holders' Representative, the Guarantors, the Trustee or any agent of the Company, the Holders' Representative, the Guarantors or the Trustee shall have any responsibility or liability to any beneficial owner of a Global Note, a member of, or a participant in, the Depositary or other Person for any aspect of the records relating to or payments made on account of beneficial ownership interests of a Global Note or maintaining, supervising or reviewing any records relating to such beneficial ownership interests.

(d) Any Note that is repurchased or owned by any Affiliate of the Company or the Guarantor (or any Person who was an Affiliate of the Company or the Guarantor at any time during the three months immediately preceding) may not be resold by such Affiliate (or such Person, as the case may be) unless registered under the Securities Act or resold pursuant to an exemption from the registration requirements of the Securities Act in a transaction that results in such Note no longer being a "restricted security" (as defined under Rule 144). The Company shall cause any Note that is repurchased or owned by it to be surrendered to the Trustee for cancellation in accordance with Section 2.08.

(e) The Trustee shall have no obligation or duty to monitor, determine or inquire as to compliance with any restrictions on transfer imposed under this Indenture or under applicable law with respect to any transfer of any interest in any Note (including any transfers between or among depositary participants or beneficial owners of interests in any Global Note) other than to require delivery of such certificates and other documentation or evidence as are expressly required by, and to do so if and when expressly required by the terms of, this Indenture, and to examine the same to determine substantial compliance as to form with the express requirements hereof.

(f) Neither the Trustee nor any agent shall have any responsibility or liability for any actions or omissions taken or not taken by the Depositary. All notices and communications to be given to the Holders and all payments to be made to the Holders in respect of the Notes shall be given or made only to, or upon the order of, the registered Holder(s) (which shall be the Depositary or its nominee in the case of a Global Note). The rights of beneficial owners in any Global Note shall be exercised only through the Depositary subject to the applicable procedures of the Depositary. The Trustee may rely and shall be fully protected in relying upon information furnished by the Depositary with respect to its members, participants and any beneficial owners.

Section 2.06. *Mutilated, Destroyed, Lost or Stolen Notes.* In case any Note shall become mutilated or be destroyed, lost or stolen, the Company in its discretion may execute, and upon receipt of a Company Order the Trustee or an authenticating agent appointed by the Trustee shall authenticate and deliver, a new Note, bearing a registration number not contemporaneously outstanding, in exchange and substitution for the mutilated Note, or in lieu of and in substitution for the Note so destroyed, lost or stolen. In every case the applicant for a substituted Note shall furnish to the Company, to the Trustee and, if applicable, to such authenticating agent such security and/or indemnity satisfactory to the Company, the Trustee, or if applicable, the authenticating agent as may be required by them to save each of them harmless from any loss, liability, cost or expense caused by or connected with such substitution, and, in every case of destruction, loss or theft, the applicant shall also furnish to the Company, to the Trustee and, if applicable, to such authenticating agent evidence to their satisfaction of the destruction, loss or theft of such Note and of the ownership thereof.

The Trustee or such authenticating agent may authenticate any such substituted Note and deliver the same upon the receipt of such security and/or indemnity as the Trustee, the Company and, if applicable, such authenticating agent may require. No service charge shall be imposed by the Company, the Trustee, the Note Registrar, any co-Note Registrar or the Paying Agent upon the issuance of any substitute Note, but the Company and/or the Trustee may require a Holder to pay a sum sufficient to cover any documentary, stamp or similar issue or transfer tax required in connection therewith as a result of the name of the Holder of the new substitute Note being different from the name of the Holder of the old Note that became mutilated or was destroyed, lost or stolen. In case any Note for which aggregate Payments and Designated Default Interest equal to the Maximum Return Amount has been paid or is about to be paid shall become mutilated or be destroyed, lost or stolen, the Company may, in its sole discretion, instead of issuing a substitute Note, pay or authorize the payment of the same (without surrender thereof except in the case of a mutilated Note), as the case may be.

Every substitute Note issued pursuant to the provisions of this Section 2.06 by virtue of the fact that any Note is destroyed, lost or stolen shall constitute an additional contractual obligation of the Company, whether or not the destroyed, lost or stolen Note shall be found at any time, and shall be entitled to all the benefits of (but shall be subject to all the limitations set forth in) this Indenture equally and proportionately with any and all other Notes duly issued hereunder. To the extent permitted by law, all Notes shall be held and owned upon the express condition that the foregoing provisions are exclusive with respect to the replacement, redemption

or payment or repurchase of mutilated, destroyed, lost or stolen Notes and shall preclude any and all other rights or remedies notwithstanding any law or statute existing or hereafter enacted to the contrary with respect to the replacement, redemption or payment or repurchase of negotiable instruments or other securities without their surrender.

Section 2.07. *Temporary Notes.* Pending the preparation of Physical Notes, the Company may execute and the Trustee or an authenticating agent appointed by the Trustee shall, upon written request of the Company, authenticate and deliver temporary Notes (printed or lithographed). Temporary Notes shall be issuable in any authorized denomination, and substantially in the form of the Physical Notes but with such omissions, insertions and variations as may be appropriate for temporary Notes, all as may be determined by the Company. Every such temporary Note shall be executed by the Company and authenticated by the Trustee or such authenticating agent upon the same conditions and in substantially the same manner, and with the same effect, as the Physical Notes. Without unreasonable delay, the Company shall execute and deliver to the Trustee or such authenticating agent Physical Notes (other than any Global Note) and thereupon any or all temporary Notes (other than any Global Note) may be surrendered in exchange therefor, at each office or agency maintained by the Company pursuant to Section 4.02 and the Trustee or such authenticating agent shall authenticate and deliver, in exchange for such temporary Notes, Physical Notes with an equal aggregate Permitted Denomination. Such exchange shall be made by the Company at its own expense and without any charge therefor. Until so exchanged, the temporary Notes shall in all respects be entitled to the same benefits and subject to the same limitations under this Indenture as Physical Notes authenticated and delivered hereunder.

Section 2.08. *Cancellation of Notes Paid, Etc.* The Company shall cause all Notes surrendered for the purpose of payment, repurchase, registration of transfer or exchange, if surrendered to any Person other than the Trustee (including any of the Company's agents or the Company's or the Guarantors' respective Subsidiaries or Affiliates), to be surrendered to the Trustee for cancellation. All Notes delivered to the Trustee shall be canceled promptly by it, and no Notes shall be authenticated in exchange therefor except as expressly permitted by any of the provisions of this Indenture. The Trustee shall dispose of canceled Notes in accordance with its customary procedures and, after such disposition, shall deliver evidence of such disposition to the Company, at the Company's written request in a Company Order.

Section 2.09. *CUSIP and ISIN Numbers.* The Company in issuing the Notes may use "CUSIP" and/or "ISIN" numbers (if then generally in use), and, if so, the Trustee shall use "CUSIP" and/or "ISIN" numbers in all notices issued to Holders as a convenience to such Holders; *provided* that any such notice may state that no representation is made as to the correctness of such numbers either as printed on the Notes or on such notice and that reliance may be placed only on the other identification numbers printed on the Notes. The Company shall promptly notify the Trustee in writing of any change in the "CUSIP" and/or "ISIN" numbers.

Section 2.10. *Additional Notes; Repurchases*. The Company may, without the consent of the Holders and subject to Section 2.01, reopen this Indenture and issue additional Notes hereunder with the same terms and subject to the same limits as the Notes initially issued hereunder; *provided* that if any such additional Notes are not fungible with the Notes initially issued hereunder for U.S. securities law purposes, such additional Notes shall have one or more separate CUSIP numbers. Prior to the issuance of any such additional Notes, the Company shall deliver to the Trustee an Officer's Certificate and an Opinion of Counsel, such Officer's Certificate and Opinion of Counsel to cover such matters applicable to the issuance of additional Notes, in addition to those required by Section 15.05. In addition, the Company and/or the Guarantors may, to the extent permitted by law, and directly or indirectly (regardless of whether such Notes are surrendered to the Company or the Guarantors), repurchase Notes in the open market or otherwise, whether by the Company, the Guarantors or their respective Subsidiaries or through a private or public tender or exchange offer or through counterparties to private agreements, including by cash-settled swaps or other derivatives. The Company and the Guarantors shall cause any Notes so repurchased (other than Notes repurchased pursuant to cash-settled swaps or other derivatives) to be surrendered to the Trustee for cancellation in accordance with Section 2.08.

ARTICLE 3
SATISFACTION AND DISCHARGE

Section 3.01. *Satisfaction and Discharge.* This Indenture and the Notes shall upon request of the Company contained in an Officer's Certificate cease to be of further effect, and the Trustee, at the expense of the Company, shall execute such instruments reasonably requested by the Company acknowledging satisfaction and discharge of this Indenture and the Notes, when (a) (i) all Notes theretofore authenticated and delivered (other than (x) Notes which have been destroyed, lost or stolen and which have been replaced or paid as provided in Section 2.06 and (y) Notes for whose payment money has theretofore been deposited in trust or segregated and held in trust by the Company and thereafter repaid to the Company or discharged from such trust, as provided in Section 4.04(d)) have been delivered to the Trustee for cancellation; or (ii) the Company or the Guarantors have deposited with the Trustee or delivered to Holders, as applicable, after the Notes have become due and payable, cash sufficient, in the opinion of a nationally recognized firm of independent public accountants expressed in a written certificate delivered to the Trustee, to pay all of the outstanding Notes and all other sums due and payable under this Indenture by the Company or the Guarantors (including, to the extent applicable, the Aggregate Maximum Return Amount); and (b) the Company has delivered to the Trustee an Officer's Certificate and an Opinion of Counsel, each stating that all conditions precedent herein provided for relating to the satisfaction and discharge of this Indenture have been complied with. Notwithstanding the satisfaction and discharge of this Indenture, the obligations of the Company and the Guarantor to the Trustee under Section 7.06 shall survive.

ARTICLE 4
PARTICULAR COVENANTS

Section 4.01. *Payments and Default Interest.* Subject to Section 11.04, the Company covenants and agrees that it will cause to be paid the Payments and Default Interest on each of the Notes at the places, at the respective times and in the manner provided herein and in the Notes.

Section 4.02. *Maintenance of Office or Agency.* The Company will maintain in the United States of America an office or agency where the Notes may be surrendered for registration of transfer or exchange or for presentation for payment or repurchase ("**Paying Agent**") and where notices and demands to or upon the Company or the Guarantors in respect of the Notes, the Guarantee and this Indenture may be made. The Company will give prompt written notice to the Trustee of the location, and any change in the location, of such office or agency. If at any time the Company shall fail to maintain any such required office or agency or shall fail to furnish the Trustee with the address thereof, such presentations, surrenders, notices and demands may be made at the Corporate Trust Office or any other office or agency in the United States of America so designated by the Trustee as a place where Notes may be presented for payment or for registration of transfer.

The Company may also from time to time designate as Paying Agent or co-Note Registrars one or more other offices or agencies where the Notes may be presented or surrendered for any or all such purposes and may from time to time rescind such designations; *provided* that no such designation or rescission shall in any manner relieve the Company of its obligation to maintain an office or agency in the United States of America so designated by the Trustee as a place for such purposes. The Company will give prompt written notice to the Trustee of any such designation or rescission and of any change in the location of any such other office or agency. The term "**Paying Agent**" includes any such additional or other offices or agencies, as applicable.

The Company hereby initially designates the Trustee as the Paying Agent, Note Registrar, Custodian and the Corporate Trust Office as the office or agency in the United States of America where Notes may be surrendered for registration of transfer or exchange or for presentation for payment or repurchase and where notices and demands to or upon the Company or the Guarantors in respect of the Notes, the Guarantee and this Indenture may be made.

In acting hereunder and in connection with the Notes, the Paying Agent, the Custodian, and the Note Registrar shall act solely as agent of the Company and will not assume any fiduciary duty or obligation towards or relationship of agency or trust for or with any of the owners or Holders of the Notes.

Section 4.03. *Appointments to Fill Vacancies in Trustee's Office.* The Company, whenever necessary to avoid or fill a vacancy in the office of Trustee, will appoint, in the manner provided in Section 7.09, a trustee, so that there shall at all times be a Trustee hereunder.

Section 4.04. *Provisions as to Paying Agent.*

(a) The Company shall, on or before each due date of the Payments, Default Interest and/or Redemption Price, as applicable, on the Notes, deposit with the Paying Agent a sum sufficient to pay such Payments, Default Interest and/or Redemption Price, as applicable, and (unless such Paying Agent is the Trustee) the Company will promptly notify the Trustee in writing of any failure to take such action; *provided* that if such deposit is made on the due date, such deposit must be received by the Paying Agent by 11:00 a.m., New York City time, on such date; provided, further, that to the extent such deposit is received by the Paying Agent after 11:00 a.m. New York City time, on any such due date, such deposit will be deemed deposited on the next Business Day.

(b) If the Company shall appoint a Paying Agent other than the Trustee, the Company will cause such Paying Agent to execute and deliver to the Trustee an instrument in which such agent shall agree with the Trustee, subject to the provisions of this Section 4.04:

(i) that it will hold all sums held by it as such agent for the payment of the Payments and Default Interest on the Notes in trust for the benefit of the Holders of the Notes;

(ii) that it will give the Trustee prompt written notice of any failure by the Company to make any payment of the Payments and Default Interest on the Notes when the same shall be due and payable; and

(iii) that at any time during the continuance of an Event of Default, upon request of the Trustee, it will forthwith pay to the Trustee all sums so held in trust.

(c) If the Company shall act as its own Paying Agent, it will, on or before each due date of the Payments and/or Default Interest, or the Redemption Price, as applicable, on the Notes, set aside, segregate and hold in trust for the benefit of the Holders of the Notes a sum sufficient to pay such Payments and/or Default Interest, or the Redemption Price, as applicable, and will promptly notify the Trustee in writing of any failure to take such action and of any failure by the Company to make any payment of the Payments and/or Default Interest, or the Redemption Price, as applicable, on the Notes when the same shall become due and payable.

(d) Anything in this Section 4.04 to the contrary notwithstanding, the Company may, at any time, for the purpose of obtaining a satisfaction and discharge of this Indenture, or for any other reason, pay, cause to be paid or deliver to the Trustee all sums or amounts held in trust by the Company or any Paying Agent hereunder as required by this Section 4.04, such sums or amounts to be held by the Trustee upon the trusts herein contained and upon such payment or delivery by the Company or any Paying Agent to the Trustee, the Company or such Paying Agent shall be released from all further liability but only with respect to such sums or amounts.

(e) Subject to applicable abandoned property laws, any money deposited with the Trustee or any Paying Agent, or then held by the Company, in trust for the payment of the Payments and/or Default Interest, or the Redemption Price, as applicable, on any Note and

remaining unclaimed for two years shall be paid to the Company on request of the Company contained in an Officer's Certificate, or (if then held by the Company) shall be discharged from such trust; and the Holder of such Note shall thereafter, as an unsecured general creditor, look only to the Company and the Guarantors for payment thereof, and all liability of the Trustee or such Paying Agent with respect to such trust money, and all liability of the Company as trustee thereof, shall thereupon cease.

(f) Upon the occurrence of any Event of Default specified in Section 6.01(d) or Section 6.01(e), the Trustee shall automatically be the Paying Agent.

Section 4.05. *Existence.* Subject to Article 11, the Company and the Guarantors shall do or cause to be done all things necessary to preserve and keep in full force and effect its corporate existence.

Section 4.06. *Rule 144A and Rule 144 Information Requirement.* At any time the Parent Guarantor is not subject to Section 13 or 15(d) of the Exchange Act, the Parent Guarantor shall, so long as any of the Notes shall, at such time, constitute "restricted securities" within the meaning of Rule 144(a)(3) under the Securities Act, promptly provide to the Trustee and will, upon written request, provide to any Holder, beneficial owner or prospective purchaser of such Notes, the information required to be delivered pursuant to Rule 144A(d)(4) under the Securities Act to facilitate the resale of such Notes pursuant to Rule 144A and the information required to be delivered pursuant to Rule 144(c) under the Securities Act to facilitate the resale of such Notes pursuant to Rule 144.

Section 4.07. *Stay, Extension and Usury Laws.* Each of the Company and each Guarantor covenants (to the extent that it may lawfully do so) that it shall not at any time insist upon, plead, or in any manner whatsoever claim or take the benefit or advantage of, any stay, extension or usury law or other law that would prohibit or forgive the Company from paying all or any portion of the Payments for or any Default Interest on the Notes as contemplated herein, wherever enacted, now or at any time hereafter in force, or that may affect the covenants or the performance of this Indenture; and each of the Company and each Guarantor (to the extent it may lawfully do so) hereby expressly waives all benefit or advantage of any such law, and covenants that it will not, by resort to any such law, hinder, delay or impede the execution of any power herein granted to the Trustee, but will suffer and permit the execution of every such power as though no such law had been enacted.

Section 4.08. *Further Instruments and Acts.* Upon request of the Trustee, the Company will execute and deliver such further instruments and do such further acts as may be reasonably necessary or proper to carry out more effectively the purposes of this Indenture.

Section 4.09. *Compliance Certificate; Statements as to Defaults.* The Company shall deliver to the Trustee within 120 days after the end of each fiscal year of the Parent Guarantor (beginning with the fiscal year ending on December 31, 2020) an Officer's Certificate stating (i) that a review has been conducted of the activity by the Company and the Guarantors and their

respective performances under this Indenture, the Guarantee and the Notes and (ii) whether the signers thereof have knowledge of any noncompliance with the conditions and covenants under this Indenture that has occurred during the previous year and, if so, specifying each such noncompliance and the nature thereof.

Section 4.10. *Tax Matters; Organizational Limitations.*

(a) At all times at which any Note is outstanding, the Parent Guarantor shall (i) maintain, directly or indirectly, 100% equity ownership of the Company and the Subsidiary Guarantors, and (ii) cause the Company to elect to be treated as a disregarded entity for U.S. federal income tax purposes (and, in each case, neither the Guarantor nor the Company shall take any action that is inconsistent with the foregoing); provided that if the Company is held indirectly by the Guarantor, the Company shall be considered as disregarded as a separate entity from the Guarantor for U.S. federal income tax purposes.

(b) The Parent Guarantor shall, within sixty (60) days of the end of the Parent Guarantor's taxable year, inform any Holder that is also a shareholder, in writing, whether the Parent Guarantor or any of its subsidiaries is a "passive foreign investment company" (a "**PFIC**") under Section 1297 of the U.S. Internal Revenue Code of 1986, as amended (the "**Code**") and shall also provide, upon reasonable request by any of such Holder, information necessary for such Holder to make its own independent determination as to whether the Parent Guarantor or any of its subsidiaries is a PFIC.

(c) The Parent Guarantor shall, and/or shall cause an applicable subsidiary, for the year that it is determined that the Parent Guarantor and/or such subsidiary is a PFIC and each subsequent year, to timely provide any Holder that is also a shareholder with a properly completed and duly executed "PFIC Annual Information Statement" that meets the requirements of Section 1.1295-1(g) of the U.S. Department of the Treasury regulations (the "**Treasury Regulations**") and any other information or assistance required by such regulations for such Holder or its direct or indirect owners to (i) make a timely election to treat such entity that is a PFIC as a "qualified electing fund" under Section 1295 of the Code and (ii) timely fulfill its annual election requirements (as described in Section 1.1295-1(f) of the Treasury Regulations) in each subsequent year in which such Holder owns an interest (directly or indirectly) in such entity that is a PFIC.

(d) Within sixty (60) days of the end of the Parent Guarantor's taxable year, any time that there is a change in the ownership structure of either the Parent Guarantor, or any of its subsidiaries, and at any other time reasonably requested by any Holder that is also a shareholder, the Parent Guarantor shall supply such a requesting Holder with the information in its possession or that it can reasonably obtain that may be relevant to determine (i) whether such Holder, or one of its direct or indirect owners, is a "United States Shareholder" (as described in Section 951(b) of the Code) with respect to the Parent Guarantor or any of its subsidiaries, (ii) whether the Parent Guarantor, or any of its subsidiaries, is a "controlled foreign corporation" (as described in Section 957 of the Code) and (iii) such Holder's share of any income of the Parent Guarantor or

any of its subsidiaries includable in the income of a United States Shareholder under Sections 951 or 951A of the Code.

(e) The Parent Guarantor shall cooperate, and shall cause each of its subsidiaries to cooperate, with any Holder that is also a shareholder in providing such Holder with any information in its possession or that it can reasonably obtain that may be useful to such Holder to timely make all filings, returns, reports, forms or calculations as may be required for such Holder and its direct and indirect owners to comply with the provisions of the Code or any other tax law that such Holder or its direct or indirect owners are subject, including, but not limited to promptly delivering to such Holder any information regarding the Parent Guarantor or a subsidiary requested by such Holder that is in the Parent Guarantor's possession or that it can reasonably obtain. Nothing in this clause shall in any way limit the obligations of the Parent Guarantor described in this Section.

(f) Each of the Parent Guarantor and the Company agree to use commercially reasonable efforts to avoid the incurrence of any income that is effectively connected with the conduct of a trade or business within the United States within the meaning of Section 864 of the Code ("**ECI**"). If either the Parent Guarantor or the Company reasonably determines that the Parent Guarantor or the Company, as applicable, may incur ECI, it shall promptly notify the Holders and shall consider alternative structures in order to avoid or minimize any such potential ECI.

(g) Any obligation of the Parent Guarantor or the Company to provide any notification or information to a Holder pursuant to this Section shall be deemed to be satisfied if the Parent Guarantor posts such notification or information on its public website.

Section 4.11. *Certain Negative Covenants of the Company and the Guarantor.* As long as any Notes remain outstanding, none of the Guarantors or any of their Subsidiaries shall take any of the actions set forth in clauses (a) through (f) of this Section 4.11 (the "**Restricted Actions**"), unless the Parent Guarantor shall have (i) provided at least 10 days' prior written notice thereof to the Holders (including the Major Investors), and (ii) obtained the prior written consent (evidenced as provided in Article 8) of the Majority Holders; provided, that notwithstanding receipt of such consent of the Majority Holders, if prior to the expiration of such 10 day period the Major Investors cause a Veto Notice to be delivered to the Parent Guarantor, none of the Guarantors or any of their Subsidiaries shall take the applicable Restricted Action. For purposes of this Indenture, a "**Veto Notice**" means a written notice delivered to the Parent Guarantor stating that one or more Restricted Actions has been vetoed, with such notice being executed by holders of at least 30% of the outstanding Notes which must include the Major Investors so long as the Major Investors (collectively and together with their Affiliates) own at least 10% of the outstanding Notes.

(a) (i) sell, transfer or assign any assets that are material to the business of the Parent Guarantor and its Subsidiaries, taken as a whole, other than (A) sales, transfers or assignments of assets as among the Company and any Guarantor or among Guarantors, (B) sales of inventory in

the ordinary course of the business of the Parent Guarantor and its Subsidiaries, (C) pursuant to dispositions of obsolete, surplus or worn out assets that are no longer useful in conduct of the business of the Parent Guarantor and its Subsidiaries, (D) transactions wholly outside the United States involving development, marketing, distribution, services, sponsored research, collaboration, technology licensing or co-promotion agreements, strategic alliances or other non-U.S. corporate partnering transactions, and including sub-licensing or assignment of any non-U.S. rights under the Pfizer License; or (E) sales of other assets (but excluding any asset the sale of which would be reasonably expected to reduce the amount of any Payment below the reasonably expected amount of such Payment absent such sale) in an aggregate amount representing 25% of the Parent Guarantor's and its Subsidiaries consolidated assets, as reflected on the Parent Guarantor's most recent audited balance sheet, during the subsequent fiscal year of the Parent Guarantor or (ii) sell, transfer, assign or enter into any exclusive license with respect to the rights of the Guarantors to any Products, other than a transaction that complies with Article 11 hereof, or a sale pursuant to subsection (i)(A), (B), (D) or (E);

(b) permit the Company, the Subsidiary Guarantors, or any other Significant Subsidiary to undergo a Change of Control, other than in connection with a Change of Control of the Parent Guarantor;

(c) agree to the creation of any lien or encumbrance on any of its assets that would reasonably be expected to reduce the amount of any Payment below the reasonably expected amount of such Payment prior to the creation of such lien or encumbrance;

(d) sell, transfer or assign any rights to receive payments of royalties or license fees included in the calculation of Net Revenues (i) in connection with a financing transaction, or (ii) in a manner that would reasonably be expected to reduce the amount of Net Revenues or Payments below the reasonably expected amount of Net Revenues or Payments, as applicable, prior to the taking of such action; *provided, however*, that this Section 4.11(d) shall not apply to any current or future payment obligations pursuant to the Pfizer License; *provided*, *further*, that clause (i) of this Section 4.11(d) shall not apply to any liens or security interests granted in the Company's or the Guarantors' assets, so long as such liens and security interests do not limit the Company's or the Guarantors' performance of their obligations under this Indenture and the Notes;

(e) enter into any amendment of, waive any rights under, agree to the termination of any rights or provisions under, or agree to the assignment of any rights or delegation of duties under, the Pfizer Agreement if such amendment, waiver, termination, assignment or delegation could reasonably be expected to reduce the amount of Net Revenues or Payments below the reasonably expected amount of Net Revenues or Payments, as applicable, prior thereto; or

(f) take any other action outside the ordinary course of the business of the Parent Guarantor and its Subsidiaries that, directly or indirectly, would reasonably be expected to reduce the amount of Net Revenues or Payments below the reasonably expected amount of Net Revenues or Payments, as applicable, prior to the taking of such action.

Section 4.12. *Confidentiality.* The Holders' Representative hereby agrees that any confidential or non-public information it receives from or on behalf of the Company or the Guarantors or any of their respective Affiliates, which receipt arises out of the transactions contemplated by this Indenture (the "**Confidential Information**"), shall: (a) not be used for any purpose other than for purposes permitted under this Indenture; (b) not be used directly or indirectly in any way that is for competitive purposes; and (c) not be disclosed by, and shall be kept confidential by, the Holders' Representative and its respective directors, officers, members, managers, employees, affiliates and agents (collectively, "**Representatives**"); provided, however, that any such Confidential Information may be disclosed (1) to the extent necessary to prepare, prosecute and/or defend any judicial or administrative proceeding, (2) only to the Representatives of the recipient party who (i) need to know such Confidential Information and (ii) are bound in writing to a non-disclosure agreement no less restrictive than this Section 4.12, or (3) by the Holders' Representative to the Holders to the extent necessary in connection with the performance of the Holders' Representative's obligations hereunder. It is understood that such Representatives shall be informed by the Holders' Representative of the confidential nature of such Confidential Information, and that the Holders' Representative (on behalf of the Holders) shall be responsible for any disclosure or use made by its Representatives in breach of obligations under this Indenture to the same extent as if such disclosure or use had been made directly by the Holders' Representative. "Confidential Information" shall not include any information that is (A) publicly available other than because of or related to any disclosure by the Holders' Representative or any of its Representatives or (B) is lawfully disclosed to the Holders' Representative by sources (other than the Company, the Guarantor or their respective Affiliates) rightfully in possession of the Confidential Information on a non-confidential basis. If the Holders' Representative or its Representatives are legally required or requested to disclose any Confidential Information, they will in advance of such disclosure, unless otherwise prohibited by law, promptly notify the Company of such request or requirement so that the Company may, at its sole cost and expense, seek to avoid or minimize the required disclosure and/or obtain an appropriate protective order or other appropriate relief to ensure that any Confidential Information so disclosed is maintained in confidence to the maximum extent possible by the person receiving the disclosure, or, in the Company's discretion, to waive compliance with the provisions of this Indenture. In any such case, the Holders' Representative agrees to cooperate and use reasonable efforts, in each case at the Company's sole cost and expense, to avoid or minimize the required disclosure and/or obtain such protective order or other relief. If, in the absence of a protective order or the receipt of a waiver hereunder, the Holders' Representative or its Representatives are legally obligated to disclose any Confidential Information, they will disclose only so much thereof to the party compelling disclosure as they believe in good faith, on the basis of advice of counsel, is required by law. The Holders' Representative shall give the Company prior written notice of the specific Confidential Information that they believe they are required to disclose under such circumstances. All Confidential Information disclosed by or on behalf of the Company or the Guarantors or any of their respective Affiliates shall be, and shall remain, the property of the Company, the Guarantors or such Affiliate, respectively.

Section 4.13. *Books and Records.* The Company and the Guarantors shall keep, and shall cause their respective Subsidiaries to keep, true, complete and accurate records in sufficient

detail to enable the amounts payable under this Indenture to be determined by the Holders or the Holders' Representative and their consultants or professional advisors, for a period of five (5) years following the applicable Payment Date or other date on which such amounts are due and payable.

Section 4.14. *Efforts.* Guarantors shall use Diligent Efforts to generate Net Revenues and cause the Payments to achieve the Maximum Return Amount prior to the End Date.

Section 4.15. *Tax Treatment*. If the Company determines that the Notes are no longer permitted or expected to be treated for U.S. federal income tax purposes as described in Section 1.02, the Company agrees to promptly notify each Holder in writing of such determination.

Section 4.16. *Listing* . The Company shall use commercially reasonable efforts to cause the Notes and/or interests in any Global Notes to be listed on the Bermuda Stock Exchange prior to April 30, 2020 and to remain so listed until no Notes remain outstanding. Notwithstanding the foregoing, in the event that no withholding or deduction for or on account of applicable taxes by the United States, Ireland or Bermuda is reasonably expected to be required on payments and/or deliveries on the Notes if the Notes are not so listed, the Company will be under no obligation to so list (or maintain the listing of) them on any stock exchange.

Section 4.17. *Payment for Consent*. The Company and the Guarantors shall not, and shall not cause or permit any of their Subsidiaries to, directly or indirectly, pay or cause to be paid any consideration, whether by way of interest, fee or otherwise, to any Holder of any Notes for or as an inducement to any consent, waiver or amendment of any of the terms or provisions of this Indenture, the Notes, the Guarantees or the Investor Rights Agreement unless such consideration is offered to be paid (or agreed to be paid) and is paid to all Holders which so consent, waive or agree to amend in the time frame set forth in solicitation documents relating to such consent, waiver or agreement.

ARTICLE 5
LISTS OF HOLDERS AND REPORTS BY THE COMPANY AND THE TRUSTEE

Section 5.01. *Lists of Holders.* The Company covenants and agrees that it will, in accordance with Section 312 of the Trust Indenture Act, furnish or cause to be furnished to the Trustee or any Paying Agent, twice annually, not more than 15 days prior to June 30 and December 31 in each year beginning with June 30, 2020, and at such other times as the Trustee may request in writing, within 30 days after receipt by the Company of any such request (or such lesser time as the Trustee may reasonably request in order to enable it to timely provide any notice to be provided by it hereunder), a list in such form as the Trustee may reasonably require of the names and addresses of the Holders as of a date not more than 15 days (or such other date as the Trustee may reasonably request in order to so provide any such notices) prior to the time such information is furnished, except that no such list need be furnished so long as the Trustee is acting as Note Registrar.

Section 5.02. *Preservation and Disclosure of Lists; Communications to Holders*.

(a) The Trustee shall preserve, in as current a form as is reasonably practicable, all information as to the names and addresses of the Holders contained in the most recent list furnished to it as provided in Section 5.01 or maintained by the Trustee in its capacity as Note Registrar, if so acting. The Trustee may destroy any list furnished to it as provided in Section 5.01 upon receipt of a new list so furnished.

(b) The rights of the Holders to communicate with other Holders with respect to their rights under this Indenture and the corresponding rights and privileges of the Trustee shall be as provided by Section 312(b)(2) of the Trust Indenture Act, if applicable.

(c) Every Holder of Notes, by receiving and holding the same, agrees with the Company and the Trustee that neither the Company nor the Trustee shall be deemed to be in violation of law or held accountable by reason of the disclosure of any such information as to the names and addresses of the Holders made pursuant to the Trust Indenture Act (if applicable) regardless of the source from which such information was derived.

Section 5.03. *Reports by Trustee*.

(a) Within 90 days after May 15 of each year commencing with the May 15 following the date of this Indenture, the Trustee shall transmit to all Holders such reports concerning the Trustee and its actions under this Indenture as may be required pursuant to the Trust Indenture Act to the extent and in the manner provided pursuant thereto and shall send a copy of any such report to the Holders' Representative. The Trustee shall also comply with Section 313(b)(2) of the Trust Indenture Act, if applicable. The Trustee shall also deliver all reports as required by Section 313(c) of the Trust Indenture Act, if applicable.

(b) A copy of each such report shall, at the time of such transmission to the Holders, be filed by the Trustee with each stock exchange, if any, upon which the Notes are listed, with the Commission and also with the Company and the Holders' Representative. The Company will promptly notify the Trustee when the Notes are listed on any stock exchange.

Section 5.04. *Reports by the Company*.

(a) Each of the Guarantors and the Company covenants to comply with Section 314(a) of the Trust Indenture Act insofar as it relates to information, documentation and other reports which such Guarantor or the Company may be required to file with the Commission pursuant to Section 13 or Section 15(d) of the Exchange Act.

(b) The Company shall file with the Trustee, within 15 days after the same are filed with the Commission, copies of any documents or reports that the Parent Guarantor is required to file with the Commission pursuant to Section 13 or 15(d) of the Exchange Act (excluding any such information, documents or reports, or portions thereof, subject to confidential treatment and any correspondence with the Commission). Any such document or report that the Parent

Guarantor files with the Commission via the Commission's EDGAR system shall be deemed to be filed with the Trustee for purposes of this Section 5.04(b) at the time such documents are filed via the EDGAR system, it being understood that the Trustee shall not be responsible for determining whether such filings have been made.

(c) Within 75 days after the end of each Payment Measuring Period, the Company shall deliver to the Holders' Representative a Payment Statement with respect to such Payment Measuring Period.

(d) Delivery of the reports and documents described in subsection (b) above to the Trustee is for informational purposes only, and the Trustee's receipt of such shall not constitute constructive notice of any information contained therein or determinable from information contained therein, including the Company's or any Guarantor's compliance with any of its covenants hereunder (as to which the Trustee is entitled to conclusively rely on an Officer's Certificate).

ARTICLE 6
DEFAULTS AND REMEDIES

Section 6.01. *Events of Default.* Each of the following events shall be an "**Event of Default**" with respect to the Notes:

(a) default in any Payment or Default Interest on any Note when due and payable, and the default continues for a period of 30 days after the Company's receipt of written notice from the Trustee or the Holders of Notes representing the right to receive at least 25% of the Aggregate Principal Amount, on the terms and conditions set forth herein;

(b) failure by the Company or any Guarantor to comply with their respective obligations under Article 11;

(c) failure by the Company or any Guarantor, for 30 days after the Company's receipt of written notice from the Trustee or the Holders of Notes representing the right to receive at least 25% of the Aggregate Principal Amount, on the terms and conditions set forth herein, to comply with any of their respective other agreements contained in the Notes, the Guarantee or this Indenture;

(d) any Guarantor, the Company or any Significant Subsidiary shall commence a voluntary case or other proceeding seeking liquidation, reorganization or other relief with respect to any such Guarantor, the Company or any such Significant Subsidiary or its debts under any bankruptcy, insolvency or other similar law now or hereafter in effect or seeking the appointment of a trustee, receiver, liquidator, custodian or other similar official of any such Guarantor, the Company or any such Significant Subsidiary or any substantial part of its property, or shall consent to any such relief or to the appointment of or taking possession by any such official in an

involuntary case or other proceeding commenced against it, or shall make a general assignment for the benefit of creditors, or shall fail generally to pay its debts as they become due;

(e) an involuntary case or other proceeding shall be commenced against any Guarantor, the Company or any Significant Subsidiary seeking liquidation, reorganization or other relief with respect to such Guarantor, the Company or such Significant Subsidiary or its debts under any bankruptcy, insolvency or other similar law now or hereafter in effect or seeking the appointment of a trustee, receiver, liquidator, custodian or other similar official of such Guarantor, the Company or such Significant Subsidiary or any substantial part of its property, and such involuntary case or other proceeding shall remain undismissed and unstayed for a period of 30 consecutive days; or

(f) the Guarantee shall be held in any judicial proceeding to be unenforceable or invalid or shall cease for any reason to be in full force and effect or any Guarantor, or any Person acting on behalf of any Guarantor, shall deny or disaffirm its obligations under the Indenture or the Guarantee.

Section 6.02. *Rights and Remedies on Event of Default; Suit Therefor.* If an Event of Default shall have occurred pursuant to paragraph (a) of Section 6.01, the sole remedy of the Holders of the Notes shall be to institute suit for payment of any Defaulted Amounts and any Default Interest, and no Holder shall have the right to accelerate payment of any amount in respect of the Notes, to demand payment of monetary damages other than such Defaulted Amounts and any Default Interest, or to demand payment of the Maximum Return Amount in respect of any Note prior to any date that any such amount would otherwise become due and payable in respect of such Note. The Limited Recourse Qualification in respect of each Note shall remain in effect upon the occurrence and during the continuance of any Event of Default.

In the event there shall be pending proceedings for the bankruptcy or for the reorganization of the Company, any Guarantor or any other obligor on the Notes under Title 11 of the United States Code, or any other applicable law, or in case a receiver, assignee or trustee in bankruptcy or reorganization, liquidator, sequestrator or similar official shall have been appointed for or taken possession of the Company, any Guarantor or such other obligor, the property of the Company, such Guarantor or such other obligor, or in the event of any other judicial proceedings relative to the Company, such Guarantor or such other obligor upon the Notes, or to the creditors or property of the Company, such Guarantor or such other obligor, the Trustee, irrespective of whether any payments in respect of the Notes shall then be due and payable as therein expressed and irrespective of whether the Trustee shall have made any demand pursuant to the provisions of this Section 6.02, shall be entitled and empowered, by intervention in such proceedings or otherwise, to file and prove a claim or claims in respect of the Notes, and, in case of any judicial proceedings, to file such proofs of claim and other papers or documents and to take such other actions as it may deem necessary or advisable in order to have the claims of the Trustee (including any claim for the reasonable compensation, expenses, disbursements and advances of the Trustee, its agents and counsel) and of the Holders allowed in such judicial proceedings relative to the Company, any Guarantor or any other obligor on the

Notes, its or their creditors, or its or their property, and to collect and receive any monies or other property payable or deliverable on any such claims, and to distribute the same after the deduction of any amounts due to the Trustee under Section 7.06; and any receiver, assignee or trustee in bankruptcy or reorganization, liquidator, custodian or similar official is hereby authorized by each of the Holders to make such payments to the Trustee, as administrative expenses, and, in the event that the Trustee shall consent to the making of such payments directly to the Holders, to pay to the Trustee any amount due it for reasonable compensation, expenses, advances and disbursements, including agents and counsel fees, and including any other amounts due to the Trustee under Section 7.06, incurred by it up to the date of such distribution. To the extent that such payment of reasonable compensation, expenses, advances and disbursements out of the estate in any such proceedings shall be denied for any reason, payment of the same shall be secured by a lien on, and shall be paid out of, any and all distributions, dividends, monies, securities and other property that the Holders of the Notes may be entitled to receive in such proceedings, whether in liquidation or under any plan of reorganization or arrangement or otherwise.

Nothing herein contained shall be deemed to authorize the Trustee to authorize or consent to or accept or adopt on behalf of any Holder any plan of reorganization, arrangement, adjustment or composition affecting such Holder or the rights of any Holder thereof, or to authorize the Trustee to vote in respect of the claim of any Holder in any such proceeding.

All rights of action and of asserting claims under this Indenture, or under any of the Notes, may be enforced by the Trustee without the possession of any of the Notes, or the production thereof at any trial or other proceeding relative thereto, and any such suit or proceeding instituted by the Trustee shall be brought in its own name as trustee of an express trust, and any recovery of judgment shall, after provision for the payment of the reasonable compensation, expenses, disbursements and advances of the Trustee, its agents and counsel, be for the ratable benefit of the Holders of the Notes.

In any proceedings brought by the Trustee (and in any proceedings involving the interpretation of any provision of this Indenture to which the Trustee shall be a party) the Trustee shall be held to represent all the Holders of the Notes, and it shall not be necessary to make any Holders of the Notes parties to any such proceedings.

In case the Trustee shall have proceeded to enforce any right under this Indenture and such proceedings shall have been discontinued or abandoned because of any waiver pursuant to Section 6.07 or for any other reason or shall have been determined adversely to the Trustee, then and in every such case the Company, the Guarantors, the Holders and the Trustee shall, subject to any determination in such proceeding, be restored respectively to their several positions and rights hereunder, and all rights, remedies and powers of the Company, the Guarantors, the Holders and the Trustee shall continue as though no such proceeding had been instituted.

Section 6.03. *Application of Monies Collected by Trustee.* Any monies or property collected by the Trustee pursuant to this Article 6 with respect to the Notes shall be applied in the

following order, at the date or dates fixed by the Trustee for the distribution of such monies or property, upon presentation of the several Notes, and stamping thereon the payment, if only partially paid, and upon surrender thereof, if fully paid:

First, to the payment of all amounts due the Trustee under Section 7.06 of this Indenture;

Second, to holders of Senior Debt to the extent required by Article 16;

Third, in case any Payments shall have become due and payable, and be unpaid, to the payment of (a) the Interest Payment component of such Payments, and then (b) the Principal Payment component of such Payments, in each case as described in the definition of Payments herein;

Fourth, in case any Default Interest shall have become due and payable, and be unpaid to the payment of such Default Interest; and

Fifth, to the payment of the remainder, if any, to the Company.

Section 6.04. *Proceedings by Holders.* Except to enforce the right to receive Principal Payments, Interest Payments or Default Interest when due, no Holder of any Note shall have any right by virtue of or by availing of any provision of this Indenture to institute any suit, action or proceeding in equity or at law upon or under or with respect to this Indenture, or for the appointment of a receiver, trustee, liquidator, custodian or other similar official, or for any other remedy hereunder, unless:

(a) such Holder previously shall have given to the Trustee written notice of an Event of Default and of the continuance thereof, as herein provided;

(b) Holders of Notes representing the right to receive at least 25% of the Aggregate Principal Amount, on the terms and conditions set forth herein, shall have made written request upon the Trustee to institute such action, suit or proceeding in its own name as Trustee hereunder;

(c) such Holders shall have offered to the Trustee such security and/or indemnity satisfactory to it against any loss, liability or expense to be incurred therein or thereby;

(d) the Trustee has not complied with such request for 60 days after its receipt of such notice, request and offer of security and/or indemnity; and

(e) no direction that, in the opinion of the Trustee, is inconsistent with such written request shall have been given to the Trustee by the Majority Holders within such 60-day period pursuant to Section 6.07,

(f) it being understood and intended, and being expressly covenanted by the taker and Holder of every Note with every other taker and Holder and the Trustee that no one or more

Holders shall have any right in any manner whatever by virtue of or by availing of any provision of this Indenture to affect, disturb or prejudice the rights of any other Holder, or to obtain or seek to obtain priority over or preference to any other such Holder, or to enforce any right under this Indenture, except in the manner herein provided and for the equal, ratable and common benefit of all Holders (except as otherwise provided herein), it being understood that the Trustee does not have an affirmative duty to ascertain whether or not any actions or forbearances by a Holder are prejudicial to other Holders. For the protection and enforcement of this Section 6.04, each and every Holder and the Trustee shall be entitled to such relief as can be given either at law or in equity.

Notwithstanding any other provision of this Indenture and any provision of any Note, the right of any Holder to receive payment or delivery, as the case may be, of (x) unpaid Principal Payments of, (y) accrued and unpaid Interest Payments on, and (z) accrued and unpaid Default Interest, if any, on, such Note, on or after the respective due dates expressed or provided for in such Note or in this Indenture, or to institute suit for the enforcement of any such payment or delivery, as the case may be, on or after such respective dates against the Company, shall not be impaired or affected without the consent of such Holder.

Section 6.05. *Proceedings by Trustee.* In case of an Event of Default, the Trustee may in its discretion proceed to protect and enforce the rights vested in it by this Indenture by such appropriate judicial proceedings as are necessary to protect and enforce any of such rights, either by suit in equity or by action at law or by proceeding in bankruptcy or otherwise, whether for the specific enforcement of any covenant or agreement contained in this Indenture or in aid of the exercise of any power granted in this Indenture, or to enforce any other legal or equitable right vested in the Trustee by this Indenture or by law.

Section 6.06. *Remedies Cumulative and Continuing.* Except as provided in the last paragraph of Section 2.06, all powers and remedies given by this Article 6 to the Trustee or to the Holders shall, to the extent permitted by law, be deemed cumulative and not exclusive of any thereof or of any other powers and remedies available to the Trustee or the Holders of the Notes, by judicial proceedings or otherwise, to enforce the performance or observance of the covenants and agreements contained in this Indenture, and no delay or omission of the Trustee or of any Holder of any of the Notes to exercise any right or power accruing upon any Event of Default shall impair any such right or power, or shall be construed to be a waiver of any such Event of Default or any acquiescence therein; and, subject to the provisions of Section 6.04, every power and remedy given by this Article 6 or by law to the Trustee or to the Holders may be exercised from time to time, and as often as shall be deemed expedient, by the Trustee or by the Holders.

Section 6.07. *Direction of Proceedings and Waiver of Events of Default by Majority of Holders.* The Majority Holders shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the Trustee or exercising any trust or power conferred on the Trustee with respect to the Notes; *provided*, *however*, that (a) such direction shall not be in conflict with any rule of law or with this Indenture, and (b) the Trustee may take any other action deemed proper by the Trustee that is not inconsistent with such

direction. The Trustee may refuse to follow any direction that it determines is unduly prejudicial to the rights of any other Holder (it being understood that the Trustee does not have an affirmative duty to ascertain whether or not any actions or forbearances by a Holder are prejudicial to other Holders) or that would involve the Trustee in personal liability. Prior to taking any action hereunder, the Trustee shall be entitled to indemnification and/or security from the Holders satisfactory to it against all losses, liabilities, or expenses caused by taking or not taking such action. The Majority Holders (determined in accordance with Section 8.04 and including waivers obtained in connection with a repurchase of, or tender or exchange offer for, Notes) may on behalf of the Holders of all of the Notes waive any past Event of Default hereunder and its consequences except (i) a default in the payment of accrued and unpaid Default Interest, if any, or the Principal Payments or Interest Payments on the Notes when due that has not been cured, or (ii) a default in respect of a covenant or provision hereof which under Article 10 cannot be modified or amended without the consent of each Holder of an outstanding Note affected. Upon any such waiver the Company, the Guarantors, the Trustee, the Holders' Representative and the Holders of the Notes shall be restored to their former positions and rights hereunder; but no such waiver shall extend to any subsequent or other Event of Default or impair any right consequent thereon. Whenever any Event of Default hereunder shall have been waived as permitted by this Section 6.07, said Event of Default shall for all purposes of the Notes and this Indenture be deemed to have been cured and to be not continuing.

Section 6.08. *Notice of Defaults*.

(a) Upon the Company becoming aware of the occurrence of any Event of Default or the occurrence of any event, circumstance or condition that following notice or the lapse of time provided for under Section 6.01 would constitute an Event of Default, the Company shall as soon as possible, and in any event within 15 Business Days after becoming aware of any such occurrence, file with the Trustee written notice of such Event of Default or event, circumstance or condition.

(b) The Trustee shall, within 90 days after any Event of Default for which it receives written notice as provided for in Section 6.08(a), send to all Holders as the names and addresses of such Holders appear upon the Note Register (as provided under Section 313(c) of the Trust Indenture Act, if applicable), notice of such Event of Default, unless such Event of Default or other event, circumstance or condition shall have been cured or waived before the giving of such notice.

Section 6.09. *Undertaking to Pay Costs.* All parties to this Indenture agree, and each Holder of any Note by its acceptance thereof shall be deemed to have agreed, that any court may, in its discretion, require, in any suit for the enforcement of any right or remedy under this Indenture, or in any suit against the Trustee for any action taken or omitted by it as Trustee, the filing by any party litigant in such suit of an undertaking to pay the costs of such suit and that such court may in its discretion assess reasonable costs, including reasonable attorneys' fees and expenses, against any party litigant in such suit, having due regard to the merits and good faith of the claims or defenses made by such party litigant; *provided* that the provisions of this Section

6.09 (to the extent permitted by law) shall not apply to any suit instituted by the Trustee, to any suit instituted by any Holder, or group of Holders, holding in the aggregate Notes representing the right to receive more than 10% of the Aggregate Principal Amount, on the terms and conditions set forth herein, determined in accordance with Section 8.04, or to any suit instituted by any Holder for the enforcement of the payment of the unpaid Principal Payments, accrued and unpaid Interest Payments, or accrued and unpaid Default Interest, if any, on any Note on or after the due date expressed or provided for in such Note.

ARTICLE 7
CONCERNING THE TRUSTEE

Section 7.01. *Duties and Responsibilities of Trustee.* The Trustee, prior to the occurrence of an Event of Default and after the curing or waiver of all Events of Default that may have occurred, undertakes to perform such duties and only such duties as are specifically set forth in this Indenture. In the event an Event of Default has occurred and is continuing, the Trustee shall exercise such of the rights and powers vested in it by this Indenture, and use the same degree of care and skill in its exercise, as a prudent person would exercise or use under the circumstances in the conduct of such person's own affairs; *provided* that if an Event of Default occurs and is continuing, the Trustee will be under no obligation to exercise any of the rights or powers under this Indenture at the request or direction of any of the Holders unless such Holders have offered to the Trustee indemnity and/or security satisfactory to it against any loss, liability or expense that might be incurred by it in compliance with such request or direction.

No provision of this Indenture shall be construed to relieve the Trustee from liability for its own negligent action, its own negligent failure to act or its own willful misconduct, except that:

(a) prior to the occurrence of an Event of Default and after the curing or waiving of all Events of Default that may have occurred:

(i) the duties and obligations of the Trustee shall be determined solely by the express provisions of this Indenture, and the Trustee shall not be liable except for the performance of such duties and obligations as are specifically set forth in this Indenture and no implied covenants or obligations shall be read into this Indenture against the Trustee; and

(ii) in the absence of bad faith or willful misconduct on the part of the Trustee, the Trustee may conclusively rely, as to the truth of the statements and the correctness of the opinions expressed therein, upon any certificates or opinions furnished to the Trustee and conforming to the requirements of this Indenture; but, in the case of any such certificates or opinions that by any provisions hereof are specifically required to be furnished to the Trustee, the Trustee shall be under a duty to examine the same to determine whether or not they conform to the requirements of this Indenture (but need

not confirm or investigate the accuracy of any mathematical calculations or other facts stated therein);

(b) the Trustee shall not be liable for (i) any error of judgment made in good faith by a Responsible Officer or Officers of the Trustee, unless it shall be proved that the Trustee was negligent in ascertaining the pertinent facts or (ii) any act taken or not taken hereunder in the absence of the Trustee's own negligence or willful misconduct;

(c) the Trustee shall not be liable with respect to any action taken or omitted to be taken by it in good faith in accordance with the written direction of the Majority Holders relating to the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred upon the Trustee, under this Indenture;

(d) whether or not therein provided, every provision of this Indenture relating to the conduct or affecting the liability of, or affording protection to, the Trustee shall be subject to the provisions of this Section;

(e) the Trustee shall not be liable in respect of any payment (as to the correctness of amount, entitlement to receive or any other matters relating to payment) or notice effected by the Company, any Guarantor or any Paying Agent or any records maintained by any co-Note Registrar with respect to the Notes;

(f) if any party fails to deliver a notice relating to an event the fact of which, pursuant to this Indenture, requires notice to be sent to the Trustee, the Trustee may conclusively rely on its failure to receive such notice as reason to act as if no such event occurred;

(g) in the absence of written investment direction from the Company, all cash received by the Trustee shall be placed in a non-interest bearing trust account, and in no event shall the Trustee be liable for the selection of investments or for investment losses fees, taxes or other charges incurred thereon or for losses incurred as a result of the liquidation of any such investment prior to its maturity date or the failure of the party directing such investments prior to its maturity date or the failure of the party directing such investment to provide timely written investment direction, and the Trustee shall have no obligation to invest or reinvest any amounts held hereunder in the absence of such written investment direction from the Company; and

(h) in the event that the Trustee is also acting as Custodian, Note Registrar, Paying Agent or transfer agent hereunder, the rights, protections, indemnities and immunities afforded to the Trustee pursuant to this Article 7 shall also be afforded to such Custodian, Note Registrar, Paying Agent or transfer agent.

None of the provisions contained in this Indenture shall require the Trustee to expend or risk its own funds or otherwise incur personal financial liability in the performance of any of its duties or in the exercise of any of its rights or powers.

Section 7.02. *Reliance on Documents, Opinions, Etc.* In furtherance of and subject to the Trust Indenture Act and except as otherwise provided in Section 7.01:

(a) the Trustee may conclusively rely and shall be fully protected in acting upon any resolution, certificate, statement, instrument, opinion, report, notice, request, consent, order, bond, note, coupon or other paper or document believed by it in good faith to be genuine and to have been signed or presented by the proper party or parties;

(b) any request, direction, order or demand of the Company or any Guarantor mentioned herein shall be sufficiently evidenced by an Officer's Certificate of the Company or such Guarantor, as applicable (unless other evidence in respect thereof be herein specifically prescribed); and any Board Resolution of the Company or the Guarantor may be evidenced to the Trustee by a copy thereof certified by the Secretary or an Assistant Secretary of the Company or such Guarantor, as applicable;

(c) the Trustee may consult with counsel, accountants or other relevant experts of its selection and require an Opinion of Counsel and any advice of such counsel, accountant or other relevant expert or Opinion of Counsel shall be full and complete authorization and protection from liability in respect of any action taken or omitted by it hereunder in good faith and in reliance on such advice or Opinion of Counsel;

(d) the Trustee shall not be bound to make any investigation into the facts or matters stated in any resolution, certificate, statement, instrument, opinion, report, notice, request, direction, consent, order, bond, debenture or other paper or document, but the Trustee, in its discretion, may make such further inquiry or investigation into such facts or matters as it may see fit, and, if the Trustee shall determine to make such further inquiry or investigation, it shall be entitled to examine the books, records and premises of the Company or the Guarantors, personally or by agent or attorney at the expense of the Company or the Guarantors and shall incur no liability of any kind by reason of such inquiry or investigation;

(e) the Trustee may execute any of the trusts or powers hereunder or perform any duties hereunder either directly or by or through agents, custodians, nominees or attorneys and the Trustee shall not be responsible for any misconduct or negligence on the part of any agent, custodian, nominee or attorney appointed by it with due care hereunder;

(f) the permissive rights of the Trustee enumerated herein shall not be construed as duties;

(g) the Trustee shall not be required to give any bond or surety in respect of the performance of its powers and duties hereunder;

(h) the Trustee may request that the Company or any Guarantor deliver a certificate setting forth the names of individuals and/or titles of officers authorized at such time to take specified actions pursuant to this Indenture; which certificate may be signed by any Person

authorized to sign an Officer's Certificate for the Company or the Guarantors, as applicable, including any Person specified as so authorized in any such certificate previously delivered and not superseded;

(i) the Trustee will not be responsible or liable for any action it takes or omits to take in good faith that it believes to be authorized or within the rights or powers conferred upon it by this Indenture;

(j) the Trustee will be under no obligation to exercise any of the rights or powers vested in it by this Indenture at the request or direction of any of the Holders unless such Holders have offered to the Trustee indemnity and/or security satisfactory to the Trustee against the losses, liabilities and expenses that might be incurred by it in compliance with such request or direction; and

(k) if at any time the Trustee is served with any judicial or administrative order, judgment, decree, writ or other form of judicial or administrative process which in any way affects this Indenture, the Notes or funds held by it (including orders of attachment or garnishment or other forms of levies or injunctions), the Trustee is authorized to comply therewith in any manner as it or its legal counsel of its own choosing deems appropriate; and if the Trustee complies with any such judicial or administrative order, judgment, decree, writ or other form of judicial or administrative process, the Trustee shall not be liable to any of the parties hereto or to any other person or entity even though such order, judgment, decree, writ or process may be subsequently modified or vacated or otherwise determined to have been without legal force or effect.

In no event shall the Trustee be liable or responsible for any special, indirect, consequential or punitive loss or damage of any kind whatsoever (including but not limited to lost profits), even if the Trustee has been advised of the likelihood of such loss or damage and regardless of the form of action other than any such loss or damage caused by the Trustee's willful misconduct or negligence. The Trustee shall not be charged with knowledge of any Event of Default with respect to the Notes, unless either (1) a Responsible Officer shall have actual knowledge of such Event of Default (in the case of an Event of Default pursuant to Section 6.01(a) hereof only) or (2) written notice of such Event of Default shall have been received by a Responsible Officer of the Trustee at the Corporate Trust Office and such notice references the Notes, the Company, Guarantors, and this Indenture. The rights, privileges, protections, immunities and benefits given to the Trustee, including its right to be indemnified, are extended to, and shall be enforceable by, the Trustee in each of its capacities hereunder, and each agent, custodian and other Person employed to act hereunder.

Section 7.03. *No Responsibility for Recitals, Etc.* The recitals contained herein and in the Notes (except in the Trustee's certificate of authentication) shall be taken as the statements of the Company and the Guarantors, and the Trustee assumes no responsibility for the correctness of the same. The Trustee makes no representations as to the validity or sufficiency of this Indenture, of the Guarantee or of the Notes. The Trustee shall not be accountable for the use or

application by the Company of any Notes or the proceeds of any Notes authenticated and delivered by the Trustee in conformity with the provisions of this Indenture.

Section 7.04. *Trustee, Paying Agents or Note Registrar May Own Notes.* The Trustee, any Paying Agent, or Note Registrar, in its individual or any other capacity, may become the owner or pledgee of Notes with the same rights it would have if it were not the Trustee, Paying Agent or Note Registrar.

Section 7.05. *Monies to Be Held in Trust.* All monies received by the Trustee shall, until used or applied as herein provided, be held in trust for the purposes for which they were received. Money held by the Trustee in trust hereunder need not be segregated from other funds or property except to the extent required by law. The Trustee shall be under no liability for any interest on any money received by it hereunder except as may be agreed from time to time by the Company and the Trustee.

Section 7.06. *Compensation and Expenses of Trustee.* The Company, Parent Guarantor, Iterum U.S. Limited and Iterum U.S. Holding, jointly and severally covenant and agree to pay to the Trustee, in any capacity under this Indenture, from time to time, and the Trustee shall be entitled to, compensation for all services rendered by it hereunder in any capacity (which shall not be limited by any provision of law in regard to the compensation of a trustee of an express trust) as mutually agreed to in writing between the Trustee and the Company, and the Company will pay or reimburse the Trustee upon its request for all reasonable expenses, disbursements and advances reasonably incurred or made by the Trustee in accordance with any of the provisions of this Indenture in any capacity thereunder (including the reasonable compensation and the expenses and disbursements of its agents, accountants, experts and counsel and of all Persons not regularly in its employ). The Company, Parent Guarantor, Iterum U.S. Limited and Iterum U.S. Holding, jointly and severally, covenant to indemnify the Trustee (which for purposes of this Section 7.06 shall include its officers, directors, employees, successors, assigns, agents, successors and assigns) in any capacity under this Indenture and any other document or transaction entered into in connection herewith and its agents and any authenticating agent for, and to hold them harmless against, any loss, claim (whether asserted by the Company, any Guarantor, a Holder or any Person), damage, liability or expense incurred without negligence or willful misconduct on the part of the Trustee, its officers, directors, agents or employees, or such agent or authenticating agent, as the case may be, as determined by a final, non-appealable decision of a court of competent jurisdiction, and arising out of or in connection with the acceptance or administration of this Indenture or in any other capacity hereunder, including the costs and expenses of defending themselves against any claim of liability brought by a party hereto, incurred by it in connection with the administration of the Indenture and the performance of its duties, enforcing the Company's obligations hereunder or enforcing its rights to indemnification hereunder. The obligations of the Company, the Parent Guarantor, Iterum U.S. Limited and Iterum U.S. Holding under this Section 7.06 to compensate or indemnify the Trustee and to pay or reimburse the Trustee for expenses, disbursements and advances shall be secured by a senior claim to which the Notes are hereby made subordinate on all money or property held or collected by the Trustee, except, subject to the effect of Section 6.03, funds held in trust

herewith for the benefit of the Holders of particular Notes. The Trustee's right to receive payment of any amounts due under this Section 7.06 shall not be subordinate to any other liability or indebtedness of Parent Guarantor. The obligations of the Company, the Parent Guarantor, Iterum U.S. Limited and Iterum U.S. Holding under this Section 7.06 shall survive the satisfaction and discharge of this Indenture and the earlier resignation or removal or the Trustee. Neither the Company nor any Guarantor shall be required to pay for any settlement made without their consents, which consents shall not be unreasonably withheld. The indemnification provided in this Section 7.06 shall extend to the officers, directors, agents and employees of the Trustee and any successor Trustee hereunder.

Without prejudice to any other rights available to the Trustee under applicable law, when the Trustee and its agents and any authenticating agent incur expenses or render services after an Event of Default specified in Section 6.01(d) or Section 6.01(e) occurs, the expenses and the compensation for the services are intended to constitute expenses of administration under any bankruptcy, insolvency or similar laws.

Section 7.07. *Officer's Certificate as Evidence.* Except as otherwise provided in Section 7.01, whenever in the administration of the provisions of this Indenture the Trustee shall deem it necessary or desirable that a matter be proved or established prior to taking or omitting any action hereunder, such matter (unless other evidence in respect thereof be herein specifically prescribed) may, in the absence of negligence and willful misconduct on the part of the Trustee, be deemed to be conclusively proved and established by an Officer's Certificate delivered to the Trustee, and such Officer's Certificate, in the absence of negligence and willful misconduct on the part of the Trustee, shall be full warrant to the Trustee for any action taken or omitted by it under the provisions of this Indenture upon the faith thereof.

Section 7.08. *Eligibility of Trustee.* There shall at all times be a Trustee hereunder which shall be a Person that is eligible pursuant to the Trust Indenture Act to act as such. Such Person shall have a combined capital and surplus of at least the amount required under Section 310(a)(ii) of the Trust Indenture Act and together with its Affiliates, shall have a combined capital and surplus of at least $10,000,000. If such Person publishes reports of condition at least annually, pursuant to law or to the requirements of any supervising or examining authority, then for the purposes of this Section, the combined capital and surplus of such Person shall be deemed to be its combined capital and surplus as set forth in its most recent report of condition so published. If at any time the Trustee shall cease to be eligible in accordance with the provisions of this Section, it shall resign immediately in the manner and with the effect hereinafter specified in this Article.

Section 7.09. *Resignation or Removal of Trustee.*

(a) The Trustee may at any time resign by giving written notice of such resignation to the Company and by delivering notice thereof to the Holders at their addresses as they shall appear on the Note Register. Upon receiving such notice of resignation, the Company shall promptly appoint a successor trustee by written instrument, in duplicate, executed by order of the

Company's Board of Directors, one copy of which instrument shall be delivered to the resigning Trustee and one copy to the successor trustee. If no successor trustee shall have been so appointed and have accepted appointment within 60 days after the sending of such notice of resignation to the Holders, the resigning Trustee may, upon 10 Business Days' notice to the Company and the Holders and at the expense of the Company, petition any court of competent jurisdiction for the appointment of a successor trustee, or any Holder who has been a bona fide holder of a Note or Notes for at least six months may, subject to the provisions of Section 6.09, on behalf of himself or herself and all others similarly situated, petition any such court for the appointment of a successor trustee. Such court may thereupon, after such notice, if any, as it may deem proper and prescribe, appoint a successor trustee.

(b) In case at any time any of the following shall occur:

(i) the Trustee shall cease to be eligible in accordance with the provisions of Section 7.08 and shall fail to resign after written request therefor by the Company or by any such Holder, or

(ii) the Trustee shall become incapable of acting, or shall be adjudged a bankrupt or insolvent, or a receiver of the Trustee or of its property shall be appointed, or any public officer shall take charge or control of the Trustee or of its property or affairs for the purpose of rehabilitation, conservation or liquidation,

then, in either case, the Company may by a Board Resolution remove the Trustee and appoint a successor trustee by written instrument, in duplicate, executed by order of the Company's Board of Directors, one copy of which instrument shall be delivered to the Trustee so removed and one copy to the successor trustee, or, subject to the provisions of Section 6.09, any Holder who has been a bona fide holder of a Note or Notes for at least six months may, on behalf of himself or herself and all others similarly situated, petition any court of competent jurisdiction for the removal of the Trustee and the appointment of a successor trustee. Such court may thereupon, after such notice, if any, as it may deem proper and prescribe, remove the Trustee and appoint a successor trustee.

(c) The Majority Holders may at any time remove the Trustee and nominate a successor trustee that shall be deemed appointed as successor trustee unless within 10 days after notice to the Company of such nomination the Company objects thereto, in which case the Trustee so removed or any Holder, upon the terms and conditions and otherwise as in Section 7.09(a) provided, may petition any court of competent jurisdiction for an appointment of a successor trustee.

(d) Any resignation or removal of the Trustee and appointment of a successor trustee pursuant to any of the provisions of this Section 7.09 shall become effective upon acceptance of appointment by the successor trustee as provided in Section 7.10.

Section 7.10. *Acceptance by Successor Trustee.* Any successor trustee appointed as provided in Section 7.09 shall execute, acknowledge and deliver to the Company and to its

predecessor trustee an instrument accepting such appointment hereunder, and thereupon the resignation or removal of the predecessor trustee shall become effective and such successor trustee, without any further act, deed or conveyance, shall become vested with all the rights, powers, duties and obligations of its predecessor hereunder, with like effect as if originally named as Trustee herein; but, nevertheless, on the written request of the Company or of the successor trustee, the trustee ceasing to act shall, upon payment of any amounts then due it pursuant to the provisions of Section 7.06, execute and deliver an instrument transferring to such successor trustee all the rights and powers of the trustee so ceasing to act. Upon request of any such successor trustee, the Company and the Guarantors shall execute any and all instruments in writing for more fully and certainly vesting in and confirming to such successor trustee all such rights and powers. Any trustee ceasing to act shall, nevertheless, retain a senior claim to which the Notes are hereby made subordinate on all money or property held or collected by such trustee as such, except for funds held in trust for the benefit of Holders of particular Notes, to secure any amounts then due it pursuant to the provisions of Section 7.06.

No successor trustee shall accept appointment as provided in this Section 7.10 unless at the time of such acceptance such successor trustee shall be eligible under the provisions of Section 7.08.

Upon acceptance of appointment by a successor trustee as provided in this Section 7.10, each of the Company and the successor trustee, at the written direction and at the expense of the Company shall send or cause to be sent notice of the succession of such trustee hereunder to the Holders at their addresses as they shall appear on the Note Register. If the Company fails to send such notice within 10 days after acceptance of appointment by the successor trustee, the successor trustee shall cause such notice to be sent at the expense of the Company.

Section 7.11. *Succession by Merger, Etc.* Any corporation or other entity into which the Trustee may be merged or converted or with which it may be consolidated, or any corporation or other entity resulting from any merger, conversion or consolidation to which the Trustee shall be a party, or any corporation or other entity succeeding to all or substantially all of the corporate trust business of the Trustee (including the administration of this Indenture), shall be the successor to the Trustee hereunder without the execution or filing of any paper or any further act on the part of any of the parties hereto; *provided* that in the case of any corporation or other entity succeeding to all or substantially all of the corporate trust business of the Trustee such corporation or other entity shall be eligible under the provisions of Section 7.08.

In case at the time such successor to the Trustee shall succeed to the trusts created by this Indenture, any of the Notes shall have been authenticated but not delivered, any such successor to the Trustee may adopt the certificate of authentication of any predecessor trustee or authenticating agent appointed by such predecessor trustee, and deliver such Notes so authenticated; and in case at that time any of the Notes shall not have been authenticated, any successor to the Trustee or an authenticating agent appointed by such successor trustee may authenticate such Notes either in the name of any predecessor trustee hereunder or in the name of the successor trustee; and in all such cases such certificates shall have the full force which it is

anywhere in the Notes or in this Indenture provided that the certificate of the Trustee shall have; *provided*, *however*, that the right to adopt the certificate of authentication of any predecessor trustee or to authenticate Notes in the name of any predecessor trustee shall apply only to its successor or successors by merger, conversion or consolidation.

Section 7.12. *Trustee's Application for Instructions from the Company.* Any application by the Trustee for written instructions from the Company (other than with regard to any action proposed to be taken or omitted to be taken by the Trustee that affects the rights of the Holders of the Notes under this Indenture) may, at the option of the Trustee, set forth in writing any action proposed to be taken or omitted by the Trustee under this Indenture and the date on and/or after which such action shall be taken or such omission shall be effective. The Trustee shall not be liable for any action taken by, or omission of, the Trustee in accordance with a proposal included in such application on or after the date specified in such application (which date shall not be less than three Business Days after the date any officer that the Company has indicated to the Trustee should receive such application actually receives such application, unless any such officer shall have consented in writing to any earlier date), unless, prior to taking any such action (or the effective date in the case of any omission), the Trustee shall have received written instructions in accordance with this Indenture in response to such application specifying the action to be taken or omitted.

Section 7.13. *Disqualification; Conflicting Interests*.

(a) If applicable, to the extent that the Trustee or the Company determines that the Trustee has a conflicting interest within the meaning of the Trust Indenture Act, the Trustee shall immediately notify the Company of such conflict and, within 90 days after ascertaining that it has such conflicting interest, either eliminate such conflicting interest or resign to the extent and in the manner provided by, and subject to the provisions of, the Trust Indenture Act and this Indenture. The Company shall take prompt steps to have a successor appointed in the manner provided in this Indenture.

(b) If the Trustee fails to comply with Section 7.13(a), the Trustee shall, within 10 days of the expiration of such 90 day period, transmit a notice of such failure to the Holders and the Holders' Representative in the manner and to the extent provided in the Trust Indenture Act and this Indenture.

(c) If the Trustee fails to comply with Section 7.13(a) after written request therefore by the Company or any Holder, then any Holder of any Note who has been a bona fide Holder for at least six (6) months may on behalf of himself and all others similarly situated, petition any court of competent jurisdiction for the removal of such Trustee and the appointment of a successor Trustee.

Section 7.14. *Preferential Collection of Claims Against Company.* If and when the Trustee shall be or shall become a creditor, directly or indirectly, secured or unsecured, of the Company or any Guarantor (or any other obligor upon the Notes), excluding any creditor

relationship set forth in Section 311(b) of the Trust Indenture Act, if applicable, the Trustee shall be subject to the applicable provisions of the Trust Indenture Act regarding the collection of claims against the Company or such Guarantor (or any such other obligor).

ARTICLE 8
CONCERNING THE HOLDERS

Section 8.01. *Action by Holders.* Whenever in this Indenture it is provided that the Holders of Notes representing the right to receive no less than a specified percentage of the Aggregate Principal Amount, on the terms and conditions set forth herein, or the aggregate Principal Amounts for all Notes represented at a meeting of the Holders, may take any action (including the making of any demand or request, the giving of any notice, consent or waiver or the taking of any other action), the fact that at the time of taking any such action, the Holders of such specified percentage have joined therein may be evidenced (a) by any instrument or any number of instruments of similar tenor executed by Holders in person or by agent or proxy appointed in writing, or (b) by the record of the Holders voting in favor thereof at any meeting of Holders duly called and held in accordance with the provisions of Article 9, or (c) by a combination of such instrument or instruments and any such record of such a meeting of Holders. Whenever the Company or the Trustee solicits the taking of any action by the Holders of the Notes, the Company or the Trustee may, but shall not be required to, fix in advance of such solicitation, a date as the record date for determining Holders entitled to take such action. The record date if one is selected shall be not more than 15 days prior to the date of commencement of solicitation of such action.

Section 8.02. *Proof of Execution by Holders.* Subject to the provisions of Section 7.01, Section 7.02 and Section 9.05, proof of the execution of any instrument by a Holder or its agent or proxy shall be sufficient if made in accordance with such reasonable rules and regulations as may be prescribed by the Trustee or in such manner as shall be satisfactory to the Trustee. The holding of Notes shall be proved by the Note Register or by a certificate of the Note Registrar. The record of any Holders' meeting shall be proved in the manner provided in Section 9.06.

Section 8.03. *Who Are Deemed Absolute Owners.* The Company, the Trustee, any authenticating agent, any Paying Agent and any Note Registrar may deem the Person in whose name a Note shall be registered upon the Note Register to be, and may treat it as, the absolute owner of such Note (whether or not such Note shall be overdue and notwithstanding any notation of ownership or other writing thereon made by any Person other than the Company or any Note Registrar) for the purpose of receiving Principal Payments and Interest Payments and (subject to Section 2.03) any accrued and unpaid Default Interest on such Note and for all other purposes under this Indenture; and neither the Company nor the Trustee nor any Paying Agent nor any Note Registrar shall be affected by any notice to the contrary. The sole registered holder of a Global Note shall be the Depositary or its nominee. All such payments or deliveries so made to any Holder for the time being, or upon its order, shall be valid, and, to the extent of the sums so paid or delivered, effectual to satisfy and discharge the liability for monies payable or shares deliverable upon any such Note. Notwithstanding anything to the contrary in this Indenture or

the Notes, following an Event of Default, any owner of a beneficial interest in a Global Note may directly enforce against the Company, without the consent, solicitation, proxy, authorization or any other action of the Depositary or any other Person, such Holder's right to exchange such beneficial interest for a Note in certificated form in accordance with the provisions of this Indenture.

Section 8.04. *Certain Notes Disregarded*.

(a) In determining whether the Holders of Notes representing the right to receive no less than a specified percentage of the Principal Amounts for all Notes then outstanding, on the terms and conditions set forth herein, or in attendance at a meeting of the Holders have concurred in any direction, consent, waiver or other action under this Indenture, Notes that are owned by the Company, any Guarantor or any Subsidiary or Affiliate thereof (provided that no Initial Purchaser shall be considered such an Affiliate for this purpose) shall be disregarded and deemed not to be outstanding for the purpose of any such determination; provided that for the purposes of determining whether the Trustee shall be protected in relying on any such direction, consent, waiver or other action only Notes that a Responsible Officer actually knows are so owned shall be so disregarded. Notes so owned that have been pledged in good faith may be regarded as outstanding for the purposes of this Section 8.04 if the pledgee shall establish to the satisfaction of the Trustee the pledgee's right to so act with respect to such Notes and that the pledgee is not the Company, a Guarantor, or a Subsidiary or Affiliate thereof (provided that no Initial Purchaser shall be considered such an Affiliate for this purpose). In the case of a dispute as to such right, any decision or indecision by the Trustee taken upon the advice of counsel shall be full protection to the Trustee.

(b) In determining whether the Holders of Notes representing the right to receive no less than a specified percentage of the Principal Amounts for all Notes then outstanding, on the terms and conditions set forth herein, or in attendance at a meeting of the Holders have concurred in any direction, consent, waiver or other action under this Indenture, Notes that are owned by any Acquiring Person, as determined by the Board of Directors of the Company or Parent Guarantor or any Committee thereof, shall be disregarded and deemed not to be outstanding for the purpose of any such determination.

(c) Upon request of the Trustee, the Company shall furnish to the Trustee promptly an Officer's Certificate listing and identifying all Notes then outstanding, if any, known by the Company (or determined by the Board of Directors of the Company or Parent Guarantor or any Committee thereof) to be owned or held by or for the account of any of the Persons referenced in paragraphs (a) or (b) of this Section 8.04. Subject to Section 7.01, the Trustee shall be entitled to accept such Officer's Certificate as conclusive evidence of the facts therein set forth and of the fact that all Notes not listed therein are outstanding for the purpose of any such determination.

Section 8.05. *Revocation of Consents; Future Holders Bound.* At any time prior to (but not after) the evidencing to the Trustee, as provided in Section 8.01, of the taking of any action by the Holders of Notes representing the right to receive no less than a specified percentage of

the Aggregate Principal Amount, on the terms and conditions set forth herein, or the aggregate Principal Amounts for all Notes represented at a meeting of the Holders, in connection with such action, any Holder of a Note that is shown by the evidence to be included in the Notes the Holders of which have consented to such action may, by filing written notice with the Trustee at its Corporate Trust Office and upon proof of holding as provided in Section 8.02, revoke such action so far as concerns such Note. Except as aforesaid, any such action taken by the Holder of any Note shall be conclusive and binding upon such Holder and upon all future Holders and owners of such Note and of any Notes issued in exchange or substitution therefor or upon registration of transfer thereof, irrespective of whether any notation in regard thereto is made upon such Note or any Note issued in exchange or substitution therefor or upon registration of transfer thereof.

ARTICLE 9
HOLDERS' MEETINGS AND HOLDERS' REPRESENTATIVE

Section 9.01. *Purpose of Meetings.* A meeting of Holders may be called at any time and from time to time pursuant to the provisions of this Article 9 for any of the following purposes:

(a) to give any notice to the Company or to the Trustee or to give any directions to the Trustee permitted under this Indenture, or to consent to the waiving of any Event of Default hereunder (in each case, as permitted under this Indenture) and its consequences, or to take any other action authorized to be taken by Holders pursuant to any of the provisions of Article 6;

(b) to remove the Trustee and nominate a successor trustee pursuant to the provisions of Article 7;

(c) to consent to the execution of an indenture or indentures supplemental hereto pursuant to the provisions of Section 10.02; or

(d) to take any other action authorized to be taken by or on behalf of the Holders of any specified percentage or ratio of the Aggregate Principal Amount under any other provision of this Indenture or under applicable law.

Section 9.02. *Call of Meetings by Trustee.* The Trustee may at any time call a meeting of Holders to take any action specified in Section 9.01, to be held at such time and at such place as the Trustee shall determine. Notice of every meeting of the Holders, setting forth the time and the place of such meeting and in general terms the action proposed to be taken at such meeting and the establishment of any record date pursuant to Section 8.01, shall be sent to Holders of such Notes at their addresses as they shall appear on the Note Register. Such notice shall also be sent to the Company. Such notices shall be sent not less than 20 nor more than 90 days prior to the date fixed for the meeting.

Any meeting of Holders shall be valid without notice if the Holders of all Notes then outstanding are present in person or by proxy or if notice is waived before or after the meeting by

the Holders of all Notes then outstanding, and if the Company and the Trustee are either present by duly authorized representatives or have, before or after the meeting, waived notice.

Section 9.03. *Call of Meetings by Company or Holders.* In case at any time the Company, pursuant to a Board Resolution, or the Holders of Notes representing the right to receive no less than 10% of the Aggregate Principal Amount, on the terms and conditions set forth herein, shall have requested the Trustee to call a meeting of Holders, by written request setting forth in reasonable detail the action proposed to be taken at the meeting, and the Trustee shall not have sent the notice of such meeting within 20 days after receipt of such request, then the Company or such Holders may determine the time and the place for such meeting and may call such meeting to take any action authorized in Section 9.01, by sending notice thereof as provided in Section 9.02.

Section 9.04. *Qualifications for Voting.* To be entitled to vote at any meeting of Holders a Person shall (a) be a Holder of one or more Notes on the record date pertaining to such meeting or (b) be a Person appointed by an instrument in writing as proxy by a Holder of one or more Notes on the record date pertaining to such meeting. The only Persons who shall be entitled to be present or to speak at any meeting of Holders shall be the Persons entitled to vote at such meeting and their counsel and any representatives of the Trustee and its counsel and any representatives of the Company and its counsel.

Section 9.05. *Regulations.* Notwithstanding any other provisions of this Indenture, the Trustee may make such reasonable regulations as it may deem advisable for any meeting of Holders, in regard to proof of the holding of Notes and of the appointment of proxies, and in regard to the appointment and duties of inspectors of votes, the submission and examination of proxies, certificates and other evidence of the right to vote, and such other matters concerning the conduct of the meeting as it shall think fit.

The Trustee shall, by an instrument in writing, appoint a temporary chairman of the meeting, unless the meeting shall have been called by the Company or by Holders as provided in Section 9.03, in which case the Company or the Holders calling the meeting, as the case may be, shall in like manner appoint a temporary chairman. A permanent chairman and a permanent secretary of the meeting shall be elected by vote of the Holders of Notes representing the right to receive no less than a majority of the aggregate Principal Amounts for all Notes, on the terms and conditions set forth herein, represented at the meeting and entitled to vote at the meeting.

Subject to the provisions of Section 8.04, at any meeting of Holders each Holder or proxyholder shall be entitled to one vote for each multiple of the Principal Amount such Holder or proxyholder is entitled to receive in respect of the Notes held or represented by him or her; *provided*, *however*, that no vote shall be cast or counted at any meeting in respect of any Note challenged as not outstanding and ruled by the chairman of the meeting to be not outstanding. The chairman of the meeting shall have no right to vote other than by virtue of Notes held by it or instruments in writing as aforesaid duly designating it as the proxy to vote on behalf of other Holders. Any meeting of Holders duly called pursuant to the provisions of Section 9.02 or

Section 9.03 may be adjourned from time to time by the Holders of Notes representing the right to receive no less than a majority of the aggregate Principal Amounts for all Notes, on the terms and conditions set forth herein, represented at the meeting, whether or not constituting a quorum, and the meeting may be held as so adjourned without further notice.

Section 9.06. *Voting.* The vote upon any resolution submitted to any meeting of Holders shall be by written ballot on which shall be subscribed the signatures of the Holders or of their representatives by proxy and the multiple of the Principal Amount of the Notes held or represented by them. The permanent chairman of the meeting shall appoint two inspectors of votes who shall count all votes cast at the meeting for or against any resolution and who shall make and file with the secretary of the meeting their verified written reports in duplicate of all votes cast at the meeting. A record in duplicate of the proceedings of each meeting of Holders shall be prepared by the secretary of the meeting and there shall be attached to said record the original reports of the inspectors of votes on any vote by ballot taken thereat and affidavits by one or more Persons having knowledge of the facts setting forth a copy of the notice of the meeting and showing that said notice was sent as provided in Section 9.02. The record shall show the multiple of the Principal Amount of the Notes voting in favor of or against any resolution. The record shall be signed and verified by the affidavits of the permanent chairman and secretary of the meeting and one of the duplicates shall be delivered to the Company and the other to the Trustee to be preserved by the Trustee, the latter to have attached thereto the ballots voted at the meeting.

Any record so signed and verified shall be conclusive evidence of the matters therein stated.

Section 9.07. *No Delay of Rights by Meeting.* Nothing contained in this Article 9 shall be deemed or construed to authorize or permit, by reason of any call of a meeting of Holders or any rights expressly or impliedly conferred hereunder to make such call, any hindrance or delay in the exercise of any right or rights conferred upon or reserved to the Trustee or to the Holders under any of the provisions of this Indenture or of the Notes. Nothing contained in this Article 9 shall be deemed or construed to limit any Holder's actions pursuant to the applicable procedures of the Depositary so long as the Notes are Global Notes.

Section 9.08. *Appointment of Holders' Representative*.

(a) For purposes of (i) confirming or disputing the Company's calculation of Gross Revenue, Net Revenues, Default Interest or the amount of any Principal Payment or Interest Payment pursuant to this Indenture or any Note, and entering into settlements and compromises in respect of any such dispute, (ii) subject to 9.08(d), engaging counsel, accountants or other advisors in furtherance thereof, including in connection with any proceeding to resolve a dispute related to the Company's calculation of Net Revenues pursuant to this Indenture or the amount of any Principal Payment or Interest Payment, (iii) to give and receive notices, communications and consents under this Indenture on behalf of the Holders and (iv) to do any and all things and to take any and all action that the Holders' Representative, in its sole and absolute discretion,

may consider necessary or proper or convenient in connection with or to carry out the activities described in this Indentureto enforce the rights of the Holders, the Holders' Representative is hereby appointed, authorized and empowered, in each case subject to the rights and obligations of the Trustee set forth in this Indenture and the requirements of the Trust Indenture Act, and to the extent permitted by this Indenture and applicable law, including by virtue of a Holder's receipt and ownership of a Note, and without any further action of any of the Holders or the Company, to be the exclusive representative, exclusive agent and attorney-in-fact of the Holders, with full power of substitution, to make all decisions and determinations and to act (or not act) and execute, deliver and receive all agreements, documents, instruments and consents on behalf of and as agent for the Holders at any time and in connection with, and that may be necessary or appropriate to accomplish the intent and to implement the provisions of, this Indenture, and such appointment and the powers, immunities and rights to indemnification granted to the Holders' Representative Group hereunder: (a) are coupled with an interest and may not be revoked in whole or in part, (b) shall survive the death, incompetence, bankruptcy or liquidation of any Holder and shall be binding on any successor thereto and (c) shall survive the delivery of an assignment by any Holder of the whole or any fraction of his, her or its interest in the Payments. All actions taken by the Holders' Representative under this Indenture shall be binding upon each Holder and such Holder's successors as if expressly confirmed and ratified in writing by such Holder, and all defenses which may be available to any Holder to contest, negate or disaffirm the action of the Holders' Representative taken in good faith under this Indenture are waived. Notwithstanding the foregoing, the Holders' Representative shall have no obligation to act on behalf of the Holders, except as expressly provided herein. By executing this Indenture, the Holders' Representative accepts such appointment, authority and power.

(b) Neither the Holders' Representative nor any of its Affiliates, nor any of its or their members, general or limited partners, managers, directors, officers, contractors, advisors agents and employees (collectively, the "**Holders' Representative Group**"), shall be liable to any Holder for any action or failure to act in connection with the acceptance or administration of the Holders' Representative's responsibilities hereunder, unless and only to the extent such action or failure to act constitutes fraud, bad faith or willful misconduct as finally determined by a court of competent jurisdiction. The Company and each of the Holders agrees to promptly pay or procure the payment of the Holders' Representative Expenses and to indemnify the Holders' Representative Group for, and defend and hold the Holders' Representative Group harmless against, any loss, liability, claim, demand, suit, damage, fee, cost, expense, judgment, fine or amount paid in settlement arising out of or in connection with the Holders' Representative's duties under this Indenture, including the reasonable out-of-pocket costs and expenses of defending the Holders' Representative Group against any claims, charges, demands, suits or loss (collectively, the "**Holders' Representative Expenses**"); provided that the "Holders' Representative Expenses" (i) shall include the fees, disbursements and costs of counsel and other skilled professionals and costs incurred in connection with seeking recovery from insurers solely to the extent reasonably incurred and (ii) shall exclude any loss or liability of the Holders' Representative Group that has been finally determined by a court of competent jurisdiction to be a result of the Holders' Representative's fraud, bad faith or willful misconduct. Such Holders' Representative Expenses may be recovered (1) first, from the Representative Expense Fund,

(2) second, from the Company, (3) third, if after the use of commercially reasonable efforts recovery in full is not available from the Company, from any distribution of the Payments otherwise distributable to the Holders at the time of distribution, and (4) fourth if recovery in full is not readily available from any of the foregoing, directly from the Holders on a pro rata basis in accordance with the Principal Amount of Notes held by them. The Holders acknowledge that the Holders' Representative shall not be required to expend or risk its own funds or otherwise incur any financial liability in the exercise or performance of any of its powers, rights, duties or privileges or pursuant to this Indenture or the transactions contemplated hereby or thereby. For the avoidance of doubt, to the extent that any such funds or liabilities are so spent or incurred, they shall be deemed Holders' Representative Expenses and shall be subject to the repayment and indemnification provisions set forth herein. Furthermore, the Holders' Representative shall not be required to take any action unless the Holders' Representative has been provided with funds, security or indemnities which, in its determination, are sufficient to protect the Holders' Representative against the costs, expenses and liabilities which may be incurred by the Holders' Representative in performing such actions. In furtherance of the foregoing, on the date hereof, the Company has distributed or procured the distribution of $50,000 with the Holders' Representative (the "**Representative Expense Fund**") solely for use by the Holders' Representative to pay any Holders' Representative Expenses. If, at any time, the Holders' Representative provides written notice to the Company that additional amounts are reasonably required in order to pay all Holders' Representative Expenses incurred or reasonably expected to be incurred, the Company shall promptly deposit or procure the deposit of such amounts into the Representative Expense Fund. Upon the determination by the Holders' Representative, which shall be made reasonably and in good faith, that all Holders' Representative Expenses have been paid and no Holders' Representative Expenses are reasonably likely to be incurred in the future, the Holders' Representative shall promptly return all unused amounts in the Representative Expense Fund to the Company. Any such return of the Representative Expense Fund shall not relieve the Company or the Holders of their indemnification and reimbursement obligations set forth in this Section 9.08. Each of the Holders acknowledges and agrees that any transfer, sale or other disposition of Notes shall not relieve the transferring Holder of the indemnification and reimbursement obligations set forth in this Section 9.08; provided, that any such indemnification and reimbursement obligations may be transferred to an unaffiliated third party that acquires the Notes, and thereupon becomes a Holder, in a bona fide arms' length transaction.

(c) The Holders' Representative shall be entitled to: (i) rely upon any Payment Statement, (ii) rely upon any signature believed by it to be genuine, and (iii) reasonably assume that a signatory has proper authorization to sign on behalf of the applicable Holder or other party.

(d) The Holders' Representative and the Company shall reasonably consult with each other in connection with the retention of professional advisors with respect to any dispute related to the calculation of Gross Revenue, Net Revenues, Default Interest, or the amount of any Principal Payment or Interest Payment provided that no failure to so consult shall relieve any party of any indemnification or reimbursement obligation hereunder.

Section 9.09. *Information Rights of the Holders' Representative.* The Company shall deliver to the Holders' Representative on a timely basis such information in the possession, or under the control, of the Company or the Guarantors or any of their respective Subsidiaries that is required to be delivered hereunder or is otherwise reasonably requested by the Holders' Representative in order to assess the Company's compliance with the terms hereof and to determine Gross Revenue, Net Revenues, Default Interest and Principal Payments or Interest Payments for any Payment Measuring Period.

Section 9.10. *Disputes; Audits*.

(a) Without limiting the rights of the Holders' Representative (on behalf of the Holders) at law or in equity in connection with any breach of the terms of this Indenture, upon the written request of the Holders' Representative (but no more than once during any calendar year), and upon reasonable notice, the Company and the Guarantors shall provide an independent certified public accounting firm of nationally recognized standing jointly agreed upon by the Holders' Representative and the Company (failing agreement on which each shall designate an independent public accounting firm of its own selection, which firms shall in turn appoint an independent public accounting firm for such purpose) (the "**Independent Accountant**") with access during normal business hours to such of the records of the Company, the Guarantors and their respective Subsidiaries as may be reasonably necessary or appropriate to verify the accuracy of the information set forth in the Payment Statements and the figures underlying the calculations set forth therein for any period within the preceding three (3) years that has not previously been audited in accordance with this Section 9.10. The fees charged by such accounting firm shall be paid by the Company. The Independent Accountant shall disclose to the Holders' Representative any matters directly related to its findings and shall disclose whether it has determined that any statements set forth in the Payment Statements are incorrect. The Independent Accountant shall provide the Company with a copy of all disclosures made to the Holders' Representative. This covenant shall survive the termination of this Indenture for a period of one (1) year.

(b) If the Independent Accountant concludes, or it is otherwise determined, that any Principal Payment or Interest Payment and/or Default Interest should have been paid but was not paid when due, the Company shall pay each Holder the applicable amounts, plus Default Interest calculated in accordance with Section 2.03(d) on any unpaid Principal Payment or Interest Payment accruing from the date on which such Principal Payment or Interest Payment should have been paid. The Company shall pay such amount to Holders of record as of a date that is fifteen (15) days prior to a payment date selected by the Company, which payment date must be within twenty (20) days of the date the Holders' Representative delivered to the Company the Independent Accountant's written report. The decision of such Independent Accountant shall be final, conclusive and binding on the Company, the Guarantors and the Holders, shall be non-appealable and shall not be subject to further review.

(c) Upon the expiration of three (3) years following the end of any Payment Measuring Period, the calculations set forth in the corresponding Payment Statement shall be conclusive and binding on each Holder.

(d) Each Person (other than the Holders' Representative) seeking to receive information from the Company in connection with a review or audit pursuant to this Section 9.10 shall enter into, and shall cause its accounting firm or other representative to enter into, a reasonable and mutually satisfactory confidentiality agreement with the Company obligating such party to retain all such financial information disclosed to such party in confidence pursuant to such confidentiality agreement and not use such information for any purpose other than the completion of such review or audit.

(e) Neither the Company, the Parent Guarantor nor any of their respective Affiliates shall, and each shall cause its Affiliates not to, enter into any license or distribution agreement with any third party (other than the Company or its Affiliates) with respect to any Product unless such agreement contains provisions that would allow the Holders' Representative and any Independent Accountant appointed pursuant to this Section 9.10 such access to the records of the other party to such license or distribution agreement as may be reasonably necessary to perform its duties pursuant to this Indenture including this Section 9.10.

Section 9.11. *Successor Holders' Representative.* The Holders' Representative may be removed for any reason or no reason by written consent of the Majority Holders if the Major Investors collectively, and together with their Affiliates, cease to own, directly or indirectly, at least 10% of the outstanding Notes. The Holders' Representative may resign at any time upon 10 days written notice to the Company. In the event that the Holders' Representative becomes incapacitated, dissolves, or becomes otherwise ineligible or incapable of performing its responsibilities hereunder or resigns or is removed from such position, the Majority Holders shall be authorized to and shall select another representative to fill such vacancy and such substituted representative shall be deemed to be the Holders' Representative for all purposes of this Indenture. The immunities and rights to indemnification shall survive the resignation or removal of the Holders' Representative and the Closing and/or any termination of this Indenture. The newly-appointed Holders' Representative shall notify the Company, the Trustee and any other appropriate Person in writing of his or her appointment, provide evidence that the Majority Holders approved such appointment and provide appropriate contact information for purposes of this Indenture. The Company and the Trustee shall be entitled to rely upon, without independent investigation, the identity and validity of such newly-appointed Holders' Representative as set forth in such written notice. The Holders are intended third party beneficiaries of this Section 9.11. If a successor Holders' Representative is not appointed within 180 days after the Holders' Representative becomes unable to perform his, her or its responsibilities hereunder or resigns or is removed from such position, the Company shall appoint a successor Holders' Representative.

ARTICLE 10
SUPPLEMENTAL INDENTURES

Section 10.01. *Supplemental Indentures Without Consent of Holders.* The Company and the Guarantors (when authorized by the resolutions of each of their respective Boards of Directors), and the Trustee, at the Company's expense, may from time to time and at any time enter into an indenture or indentures supplemental hereto for one or more of the following purposes:

(a) to cure any ambiguity, omission, defect or inconsistency;

(b) to provide for the assumption by a Successor Company of the obligations of the Company or the Guarantors under the Notes, this Indenture or the Guarantee pursuant to Article 11;

(c) to add additional guarantees and/or guarantors with respect to the Notes;

(d) to secure the Notes;

(e) to add to the covenants or Events of Default of the Company or the Guarantors for the benefit of the Holders or surrender any right or power conferred upon the Company or the Guarantors;

(f) to make any change that does not adversely affect the rights of any Holder;

(g) to provide for the acceptance of appointment by a successor trustee pursuant to Section 7.10 or to facilitate the administration of the trusts by more than one trustee;

(h) to make any amendments or changes necessary to comply or maintain compliance with the Trust Indenture Act, if applicable;

(i) to reflect the issuance of additional Notes as permitted by the Indenture; or

(j) to make any changes or modifications necessary in connection with the registration of the Notes under the Securities Act; *provided*, *however*, that such action does not adversely affect the interests of the Holders of Notes in any material respect.

Upon the written request of the Company and subject to Section 10.05, the Trustee is hereby authorized to, and shall join with the Company and the Guarantors in the execution of any such supplemental indenture, to make any further appropriate agreements and stipulations that may be therein contained, except that the Trustee shall not be obligated to, but may, enter into any supplemental indenture that affects the Trustee's own rights, duties, privileges, liabilities or immunities under this Indenture or otherwise.

Any supplemental indenture authorized by the provisions of this Section 10.01 may be executed by the Company, the Guarantors and the Trustee without the consent of the Holders of any of the Notes at the time outstanding, notwithstanding any of the provisions of Section 10.02.

Section 10.02. *Supplemental Indentures with Consent of Holders.* With the consent (evidenced as provided in Article 8) of the Majority Holders (determined in accordance with Article 8 and including consents obtained in connection with a repurchase of, or tender or exchange offer for, Notes), the Company and the Guarantors (when authorized by the resolutions each of their respective Boards of Directors), and the Trustee, at the Company's expense, may from time to time and at any time enter into an indenture or indentures supplemental hereto for the purpose of adding any provisions to or changing in any manner or eliminating any of the provisions of this Indenture or any supplemental indenture or of modifying in any manner the rights of the Holders; *provided*, *however*, that, without the consent of each Holder of an outstanding Note affected, no such supplemental indenture shall:

(a) reduce the Payment Rate provided for in this Indenture;

(b) reduce the amount or percentage of Notes whose Holders must consent to an amendment or waive any past default;

(c) reduce the rate of Default Interest;

(d) reduce the Principal Amount of any Note;

(e) reduce the Maximum Return Amount of any Note;

(f) make any Note payable in a currency or at a place of payment other than that stated in the Note;

(g) change the definitions of "End Date", "Interest Payment", "Payment", "Payment Measuring Period", "Principal Payment", "Products", "Net Revenues" or any other defined term that is incorporated into any such definition.

(h) change any provision of this Indenture or the related definitions to affect the ranking of the Notes or any Guarantee;

(i) increase the Aggregate Principal Amount to an amount in excess of $120,000;

(j) make any change in this Article 10 that requires each Holder's consent or in the waiver provisions in Section 6.07 or any other amendment or waiver processes in this Indenture; or

(k) modify the Guarantee in any manner adverse to the Holders (including the release of any Guarantor from any of its obligations under its Guarantee or this Indenture); or

(l) make any change to Section 4.12.

Upon the written request of the Company, and upon the filing with the Trustee of evidence of the consent of Holders as aforesaid and subject to Section 10.05, the Trustee shall

join with the Company and the Guarantors in the execution of such supplemental indenture unless such supplemental indenture affects the Trustee's own rights, duties or immunities under this Indenture or otherwise, in which case the Trustee may, but shall not be obligated to, enter into such supplemental indenture.

Holders do not need under this Section 10.02 to approve the particular form of any proposed supplemental indenture. It shall be sufficient if such Holders approve the substance thereof. After any such supplemental indenture becomes effective, the Company shall deliver, or cause to be delivered, to the Holders' Representative and to the Holders a notice briefly describing such supplemental indenture. However, the failure to give such notice to the Holders' Representative, or any defect in the notice, will not impair or affect the validity of the supplemental indenture.

Section 10.03. *Effect of Supplemental Indentures.* Upon the execution of any supplemental indenture pursuant to the provisions of this Article 10, this Indenture shall be and be deemed to be modified and amended in accordance therewith and the respective rights, limitation of rights, obligations, privileges, duties and immunities under this Indenture of the Trustee, the Company, the Guarantors, the Holders and the Holders' Representative Group shall thereafter be determined, exercised and enforced hereunder subject in all respects to such modifications and amendments and all the terms and conditions of any such supplemental indenture shall be and be deemed to be part of the terms and conditions of this Indenture for any and all purposes.

Section 10.04. *Notation on Notes.* Notes authenticated and delivered after the execution of any supplemental indenture pursuant to the provisions of this Article 10 may, at the Company's expense, bear a notation in form approved by the Trustee as to any matter provided for in such supplemental indenture. If the Company or the Trustee shall so determine, new Notes so modified as to conform, in the opinion of the Trustee and the Board of Directors of the Company, to any modification of this Indenture contained in any such supplemental indenture may, at the Company's expense, be prepared and executed by the Company, authenticated, upon receipt of a Company Order by the Trustee (or an authenticating agent duly appointed by the Trustee pursuant to Section 15.10) and delivered in exchange for the Notes then outstanding, upon surrender of such Notes then outstanding.

Section 10.05. *Evidence of Compliance of Supplemental Indenture to Be Furnished to Trustee.* In addition to the documents required by Section 15.05, the Trustee shall receive an Officer's Certificate and an Opinion of Counsel and shall be fully protected in relying upon as conclusive evidence that any supplemental indenture executed pursuant hereto complies with the requirements of this Article 10 and is permitted or authorized by this Indenture and that the supplemental indenture constitutes the legal, valid and binding obligation of the Company enforceable in accordance with its terms.

Section 10.06. *Conformity with Trust Indenture Act.* Every supplemental indenture executed pursuant to this Article shall conform to the applicable requirements of the Trust Indenture Act, if any.

ARTICLE 11
CONSOLIDATION, MERGER, SALE, CONVEYANCE AND LEASE

Section 11.01. *Parent Guarantor May Consolidate, Etc. on Certain Terms.* Subject to the provisions of Section 11.02 , the Parent Guarantor shall not consolidate with, merge with or into, or sell, convey, transfer or lease all or substantially all of its properties and assets to another Person, unless:

(a) the resulting, surviving or transferee Person (the "**Successor Company**"), if not the Parent Guarantor, shall be (i) a corporation organized and existing under the laws of the United States of America, any State thereof or the District of Columbia or the Republic of Ireland or (ii) an entity organized and existing under the laws of such other jurisdiction as approved by the Majority Holders, and in each case the Successor Company (if not the Parent Guarantor) shall expressly assume, by supplemental indenture all of the obligations of the Parent Guarantor under the Notes, this Indenture and the Guarantee, as the case may be;

(b) immediately after giving effect to such transaction, no Event of Default shall have occurred and be continuing under this Indenture;

(c) immediately after giving effect to such transaction, the Parent Guarantor shall maintain, directly or indirectly, 100% equity ownership of the Company and the Subsidiary Guarantors;

(d) to the extent such transaction constitutes a Change of Control of the Parent Guarantor, the Company and the Guarantors act in accordance with Section 11.04; and

(e) in the case of a consolidation, merger, sale, conveyance, transfer or lease involving the Company or the Subsidiary Guarantors, the Successor Company is a wholly owned Subsidiary of the Parent Guarantor.

For purposes of this Section 11.01, the sale, conveyance, transfer or lease of all or substantially all of the properties and assets of one or more Subsidiaries of the Parent Guarantor to another Person, which properties and assets, if held by the Parent Guarantor instead of such Subsidiaries, would constitute all or substantially all of the properties and assets of the Parent Guarantor on a consolidated basis, shall be deemed to be the sale, conveyance, transfer or lease of all or substantially all of the properties and assets of the Parent Guarantor to another Person.

Section 11.02. *Successor Corporation to Be Substituted.* In case of any such consolidation, merger, sale, conveyance, transfer or lease and upon the assumption by the Successor Company, by supplemental indenture (if required by Section 11.01), executed and delivered to the Trustee and satisfactory in form to the Trustee, of the due and punctual payment

of the Payments for and any accrued and unpaid Default Interest on all of the Notes and the due and punctual performance of all of the covenants and conditions of this Indenture, the Notes and the Guarantee to be performed by the Company or the Guarantors, as applicable, such Successor Company (if not Company or any Guarantor, as applicable) shall succeed to and, except in the case of a lease of all or substantially all of the Company's or the Guarantors' properties and assets, shall be substituted for the Company or the Guarantor, as applicable, with the same effect as if it had been named herein as the party of the first part. Such Successor Company thereupon may cause to be signed, and may issue either in its own name or in the name of the Company any or all of the Notes issuable hereunder which theretofore shall not have been signed by the Company and delivered to the Trustee; and, upon the written order of such Successor Company instead of the Company and subject to all the terms, conditions and limitations in this Indenture prescribed, the Trustee shall authenticate and shall deliver, or cause to be authenticated and delivered, any Notes that previously shall have been signed and delivered by the Officers of the Company to the Trustee for authentication, and any Notes that such Successor Company thereafter shall cause to be signed and delivered to the Trustee for that purpose. All the Notes so issued shall in all respects have the same legal rank and benefit under this Indenture as the Notes theretofore or thereafter issued in accordance with the terms of this Indenture as though all of such Notes had been issued at the date of the execution hereof. In the event of any such consolidation, merger, sale, conveyance or transfer (but not in the case of a lease), upon compliance with this Article 11, the Person named as the "Company", the "Parent Guarantor" or a "Subsidiary Guarantor" in the first paragraph of this Indenture (or any successor that shall thereafter have become such in the manner prescribed in this Article 11), as applicable, may be dissolved, wound up and liquidated at any time thereafter and, except in the case of a lease, such Person shall be released from its liabilities as obligor or guarantor and (in the case of the Company) maker of the Notes and from its obligations under this Indenture, the Notes and the Guarantee, as the case may be.

In case of any such consolidation, merger, sale, conveyance, transfer or lease, such changes in phraseology and form (but not in substance) may be made in the Notes thereafter to be issued as may be appropriate.

Section 11.03. *Officer's Certificate and Opinion of Counsel to Be Given to Trustee.* No such consolidation, merger, sale, conveyance, transfer or lease shall be effective unless the Trustee shall receive an Officer's Certificate and an Opinion of Counsel as conclusive evidence that any such consolidation, merger, sale, conveyance, transfer or lease and any such assumption and, if a supplemental indenture is required in connection with such transaction, such supplemental indenture, complies with the provisions of this Article 11, and in the case of the Opinion of Counsel, that such supplemental indenture is the legal, valid and binding obligation of the relevant Successor Company.

Section 11.04. *Changes of Control* . The Parent Guarantor shall require the ultimate beneficial owner or beneficial owners that controls or control, as the case may be, any acquiring Person or Persons, in any transaction permitted under this Indenture which constitutes a Change of Control of the Parent Guarantor, to guarantee the obligations of the Company and the Parent

Guarantor under this Indenture and the Guarantee, as applicable, including the Company's obligation to pay Principal Payment, Interest Payments and Default Interest when due and payable, as a condition to such transaction or series of related transactions in a manner and with an effect that does not diminish the value of the Notes and replicates, to the extent reasonably practicable, the role of the Parent Guarantor in respect of this Indenture; provided that the foregoing obligation may be waived by the Majority Holders.

ARTICLE 12
IMMUNITY OF INCORPORATORS, SHAREHOLDERS, OFFICERS AND DIRECTORS

Section 12.01. *Indenture, Notes and Guarantee Solely Corporate Obligations.* No recourse for the payment of the Principal Payments or Interest Payments for, or any accrued and unpaid Default Interest on, any Note or in respect of the Guarantee, nor for any claim based thereon or otherwise in respect thereof, and no recourse under or upon any obligation, covenant or agreement of the Company or the Guarantors in this Indenture or in any supplemental indenture or in any Note or the Guarantee, nor because of the creation of any indebtedness represented thereby, shall be had against any incorporator, shareholder, employee, agent, Officer or director or Subsidiary (other than the Company or the Subsidiary Guarantors), as such, past, present or future, of the Company, the Guarantors or of any of their respective successor corporations, either directly or through the Company, the Guarantors or any successor corporation, whether by virtue of any constitution, statute or rule of law, or by the enforcement of any assessment or penalty or otherwise; it being expressly understood that all such liability is hereby expressly waived and released as a condition of, and as a consideration for, the execution of this Indenture and the issuance of the Notes and the Guarantee.

ARTICLE 13
GUARANTEE OF NOTES

Section 13.01. *Guarantee.*

(a) By its execution hereof, each Guarantor acknowledges and agrees that it receives substantial benefits from the Company and the issuance of the Notes and that such Guarantor is providing its Guarantee for good and valuable consideration, including such substantial benefits. Accordingly, subject to the provisions of this Article 13, such Guarantor hereby fully and unconditionally guarantees as a primary principal obligation and not merely as a surety to each Holder, on a senior basis, and its successors and assigns that: (x) the Principal Payments and Interest Payments (including the Redemption Price, if applicable) shall be duly and punctually paid in full and/or performed in accordance with the terms of this Indenture when due, along with any Default Interest, if any, on the Notes, (y) in case of any extension of time of payment of any Notes or any of such other obligations, the same shall be duly and punctually paid in full and/or performed in accordance with the terms of this Indenture when due or performed in accordance with the terms of the extension, along with any Default Interest, on the Notes. Furthermore, subject to the provisions of this Article 13, such Guarantor hereby unconditionally guarantees to the Trustee, the Holders' Representative and each Holder and their respective

successors and assigns that all other obligations of the Company to the Holders, the Holders' Representative or the Trustee hereunder or under the Notes (including fees, expenses or other obligations) shall be promptly paid in full or performed, all in accordance with the terms hereof, subject, however, in the case of each of the foregoing obligations set forth above in this Section 13.01, to the limitations set forth in Section 13.02 hereof (the obligations set forth in this Section 13.01 collectively, the "**Guarantee Obligations**"). Failing payment when due of any Guarantee Obligation for whatever reason, such Guarantor will be obligated to pay the same immediately. An Event of Default with respect to the Notes under this Indenture shall constitute an event of default under the Guarantee, provided that the Holders shall have no right to accelerate payment of any amount in respect of the Notes by any Guarantor. Each Guarantor covenants and agrees, and each Holder of a Note, by such Holder's acceptance thereof, likewise covenants and agrees, that, notwithstanding anything in this Indenture or the Notes to the contrary, the Guarantee constitutes a general unsecured obligation of each Guarantor and will be subordinate in right of payment to any Guarantor Senior Debt, it being understood that the terms of Article 16 of this Indenture shall apply to the Guarantee Obligations as if (i) such Article 16 were set forth herein in full, (ii) the term "Guarantee Obligations" were substituted for the term "Notes" appearing in such Article 16, (iii) the term "Guarantor Senior Debt" were substituted for the term "Senior Debt" appearing in such Article 16 and (iv) the term "Guarantors" were substituted for the term "Company" appearing in such Article 16.

(b) Subject to the provisions of this Article 13, each Guarantor hereby agrees that its Guarantee hereunder shall be unconditional, irrespective of the validity, regularity or enforceability of the Notes or this Indenture, the absence of any action to enforce the same, any waiver or consent by any Holder of the Notes with respect to any thereof, the entry of any judgment against the Company, any action to enforce the same or any other circumstance which might otherwise constitute a legal or equitable discharge or defense of such Guarantor. Such Guarantor hereby waives and relinquishes: (i) any right to require the Trustee, the Holders, the Holders' Representative or the Company (each, a "**Benefited Party**") to proceed against the Company or any other Person or to proceed against or exhaust any security held by a Benefited Party at any time or to pursue any other remedy in any secured party's power before proceeding against such Guarantor; (ii) any defense that may arise by reason of the incapacity, lack of authority, death or disability of any other Person or Persons or the failure of a Benefited Party to file or enforce a claim against the estate (in administration, bankruptcy or any other proceeding) of any other Person or Persons; (iii) demand, protest and notice of any kind (except as expressly required by this Indenture), including but not limited to notice of the existence, creation or incurring of any new or additional indebtedness or obligation or of any action or non-action on the part of such Guarantor, the Company, any Benefited Party, any creditor of such Guarantor or the Company or on the part of any other Person whomsoever in connection with any obligations the performance of which are hereby guaranteed; (iv) any defense based upon an election of remedies by a Benefited Party, including but not limited to an election to proceed against such Guarantor for reimbursement; (v) any defense based upon any statute or rule of law which provides that the obligation of a surety must be neither larger in amount nor in other respects more burdensome than that of the principal; (vi) any defense arising because of a Benefited Party's election, in any proceeding instituted under Bankruptcy Law, of the application of

Section 1111(b)(2) of the Bankruptcy Code or any similar provision (including under Bermudan or Irish law); and (vii) any defense based on any borrowing or grant of a security interest under Section 364 of the Bankruptcy Code or any similar provision (including under Bermudan or Irish law). Such Guarantor hereby covenants that, except as otherwise provided therein, the Guarantee shall not be discharged except by payment or satisfaction, as the case may be, in full of all Guarantee Obligations, including the Principal Payments, Interest Payments (including the Redemption Price, if applicable), and any Default Interest on the Notes and all other costs provided for under this Indenture (including as provided in Article 7).

(c) Each Guarantor as principal obligor and as a separate and independent obligation and liability from its other obligations and liabilities under this Indenture agrees to indemnify and keep indemnified each Holder, the Holders' Representative Group and the Trustee in full and on demand in respect of the performance and discharge of the Guarantee Obligations (except where the Company's failure to perform or discharge the Guarantee Obligations results from such Holder's failure to comply with its obligations under the Indenture or the Trustee's negligence or willful misconduct or the Company contesting any payment or part of a payment in good faith).

(d) If any Holder, the Holders' Representative or the Trustee is required by any court or otherwise to return to either the Company or any Guarantor, or any trustee or similar official acting in relation to either the Company or such Guarantor, any amount paid by the Company or such Guarantor to the Trustee, the Holders' Representative or such Holder, then the Guarantee, to the extent theretofore discharged, shall be reinstated in full force and effect. Each Guarantor agrees that it shall not be entitled to any right of subrogation in relation to the Holders or the Holders' Representative in respect of any Guarantee Obligations hereby until payment in full of all such obligations guaranteed hereby. Each Guarantor agrees that, as between it, on the one hand, and the Holders, the Holders' Representative and the Trustee, on the other hand, (x) the maturity of the obligations guaranteed hereby may be accelerated as provided in Article 6 hereof for the purposes hereof, notwithstanding any stay, injunction or other prohibition preventing such acceleration in respect of the Guarantee Obligations, and (y) in the event of any acceleration of such obligations as provided in Article 6 hereof, such Guarantee Obligations (whether or not due and payable) shall forthwith become due and payable by such Guarantor for the purpose of the Guarantee.

Section 13.02. *Limitation of the Guarantors' Liability; Certain Bankruptcy Events*.

(a) The End Date, the Limited Recourse Qualification, the Aggregate Maximum Return Amount Qualification and each applicable Maximum Return Amount Qualification shall apply to the Guarantee Obligations in the same manner and to the same extent as to the obligations of the Company under this Indenture and the Notes.

(b) Each Guarantor, and by its acceptance hereof each Holder, hereby confirms that it is the intention of all such parties that the Guarantee Obligations of the Guarantors pursuant to its Guarantee not constitute a fraudulent transfer or conveyance for purposes of any Bankruptcy

Law, the Uniform Fraudulent Conveyance Act, the Uniform Fraudulent Transfer Act or any similar federal, state or foreign law. To effectuate the foregoing intention, the Holders and the Guarantors hereby irrevocably agree that the Guarantee Obligations of the Guarantors under this Article 13 shall be limited to the maximum amount as shall, after giving effect to all other contingent and fixed liabilities of the Guarantors, result in the Guarantee Obligations of the Guarantors under the Guarantee not constituting a fraudulent transfer or conveyance.

(c) Each Guarantor hereby covenants and agrees, to the fullest extent that it may do so under applicable law, that in the event of the insolvency, examinership, bankruptcy, dissolution, liquidation or reorganization of the Company, such Guarantor shall not file (or join in any filing of), or otherwise seek to participate in the filing of, any motion or request seeking to stay or to prohibit (even temporarily) execution on the Guarantee and hereby waives and agrees not to take the benefit of any such stay of execution, whether under Section 362 or 105 of the Bankruptcy Code or otherwise.

Section 13.03. *Execution And Delivery*. The Guarantee shall be evidenced by the execution and delivery of this Indenture or a supplement to this Indenture and no notation of the Guarantee need be endorsed on any Note. Each Guarantor hereby agrees that its Guarantee set forth in Section 13.01 shall remain in full force and effect notwithstanding the absence of the endorsement of any notation of such Guarantee on the Notes. If an Officer whose signature is on this Indenture no longer holds that office at the time the Trustee authenticates the Note, the Guarantee shall be valid nevertheless. The delivery of any Note by the Trustee, after the authentication thereof hereunder, shall constitute due delivery of the Guarantee set forth in this Indenture on behalf of the Guarantors.

ARTICLE 14
OPTIONAL REDEMPTION

Section 14.01. *Optional Redemption* . No sinking fund is provided for the Notes. Subject to Section 14.04, the Company may at any time, upon receipt of written consent of the holders of the Senior Debt while the Senior Debt remains outstanding, redeem all, but not less than all, of the Notes (an "**Optional Redemption**") in exchange for cash in an amount per Note equal to the Maximum Return Amount of such Note less Principal Payments and Interest Payments made through and including the applicable Redemption Date in respect of such Note, plus any accrued but unpaid Default Interest other than Designated Default Interest made through and including the applicable Redemption Date (the "**Redemption Price**"), in all cases without any additional premium or penalty.

Section 14.02. *Notice of Optional Redemption; Selection of Notes*.

(a) In case the Company exercises its Optional Redemption right to redeem all of the Notes pursuant to Section 14.01, it shall fix a date for redemption (each, a "**Redemption Date**") and it or, at its written request received by the Trustee not less than 75 days prior to the Redemption Date (or such shorter period of time as may be acceptable to the Trustee), the

Trustee, in the name of and at the expense of the Company, shall deliver or cause to be delivered a notice of such Optional Redemption (a "**Redemption Notice**") not less than 60 nor more than 70 days prior to the Redemption Date to each Holder of Notes so to be redeemed as a whole or in part; *provided*, *however*, that, if the Company shall give such notice, it shall also give written notice of the Redemption Date to the Trustee and the Paying Agent (if other than the Trustee).

(b) The Redemption Notice, if delivered in the manner herein provided, shall be conclusively presumed to have been duly given, whether or not the Holder receives such notice. In any case, failure to give such Redemption Notice or any defect in the Redemption Notice to the Holder of any Note designated for redemption as a whole or in part shall not affect the validity of the proceedings for the redemption of any other Note.

(c) Each Redemption Notice shall specify:

(i) the Redemption Date;

(ii) the Redemption Price;

(iii) that on the Redemption Date, the Redemption Price will become due and payable upon each Note to be redeemed, and that Default Interest thereon, if any, shall cease to accrue on and after the Redemption Date;

(iv) the place or places where such Notes are to be surrendered for payment of the Redemption Price; and

(v) the CUSIP, ISIN or other similar numbers, if any, assigned to such Notes.

A Redemption Notice shall be irrevocable.

Section 14.03. *Payment of Notes Called for Redemption.*

(a) If any Redemption Notice has been given in respect of the Notes in accordance with Section 14.02, the Notes shall become due and payable on the Redemption Date at the place or places stated in the Redemption Notice and at the applicable Redemption Price. On presentation and surrender of the Notes at the place or places stated in the Redemption Notice, the Notes shall be paid and redeemed by the Company at the applicable Redemption Price.

(b) Prior to the open of business on the Redemption Date, the Company shall deposit with the Paying Agent or, if any Guarantor, the Company or a respective Subsidiary of a Guarantor or the Company is acting as the Paying Agent, shall segregate and hold in trust as provided in Section 7.05 an amount of cash (in immediately available funds if deposited on the Redemption Date), sufficient to pay the Redemption Price of all of the Notes to be redeemed on such Redemption Date. Subject to receipt of funds by the Paying Agent, payment for the Notes to be redeemed shall be made on the Redemption Date for such Notes. The Paying Agent shall,

promptly after such payment and upon written demand by the Company, return to the Company any funds in excess of the Redemption Price.

Section 14.04. *Adjustments in Connection with Change of Control*. In the event that any Redemption Date occurs (a) prior to the first date on which there has been a commercial sale of a Product in the United States following FDA Approval with respect to such Product and (b) on the date of, or within sixty (60) days following, any Change of Control of the Parent Guarantor, then the Redemption Price will be equal to (i) 50% of the Maximum Return Amount of such Note less Principal Payments and Interest Payments made through and including the applicable Redemption Date in respect of such Note, plus (ii) any accrued but unpaid Default Interest, in all cases without any additional premium or penalty.

ARTICLE 15
MISCELLANEOUS PROVISIONS

Section 15.01. *Provisions Binding on Successors.* All the covenants, stipulations, promises and agreements of each of the Company and the Guarantors contained in this Indenture shall bind its successors and assigns whether so expressed or not.

Section 15.02. *Official Acts by Successor Corporation.* Any act or proceeding by any provision of this Indenture authorized or required to be done or performed by any board, committee or Officer of the Company or any Guarantor shall and may be done and performed with like force and effect by the like board, committee or officer of any corporation or other entity that shall at the time be the lawful sole successor of the Company or such Guarantor, as the case may be.

Section 15.03. *Addresses for Notices, Etc.* Any notice or demand that by any provision of this Indenture is required or permitted to be given or made by the Trustee, by the Holders' Representative or by the Holders on the Company or the Guarantors shall be deemed to have been sufficiently given or made, for all purposes if given or made by being deposited postage prepaid by registered or certified mail in a post office letter box addressed (until another address is filed by the Company or the Guarantors with the Trustee) to Iterum Therapeutics plc, Block 2, Floor 3 Harcourt Centre, Harcourt Street, Dublin 2, Ireland, Attention: Corey Fishman, with a copy to Iterum Therapeutics plc, Legal Department, Block 2, Floor 3 Harcourt Centre, Harcourt Street, Dublin 2, Ireland. Any notice, direction, request or demand hereunder to or upon the Trustee shall be in writing (including facsimile or electronic transmission in PDF format). Notices by certified or registered mail shall be deemed to have been sufficiently given or made, for all purposes, if given or made by being deposited postage prepaid by registered or certified mail in a post office letter box addressed to the Corporate Trust Office or sent electronically in PDF format and, in each case, upon actual receipt by the Trustee.

The Trustee agrees to accept and act upon instructions or directions pursuant to this Indenture sent by unsecured e-mail, pdf, facsimile transmission or other similar unsecured electronic methods, *provided* that the Trustee shall have received an incumbency certificate

listing persons designated to give such instructions or directions and containing specimen signatures of such designated persons, which such incumbency certificate shall be amended and replaced whenever a person is to be added or deleted from the listing.

The Trustee, by notice to the Company, may designate additional or different addresses for subsequent notices or communications.

Any notice or communication given to the Holders' Representative shall be delivered solely via email or facsimile to:

Holders' Representative:

Iterum Holders' Representative LLC
c/o Sarissa Capital Management LP
660 Steamboat Road, 3rd Floor
Greenwich, CT 06830
Attention: Mark DiPaolo
E-mail: mdipaolo@sarissacap.com

with copies (which will not constitute notice) to:

Willkie Farr & Gallagher LLP
787 Seventh Avenue
New York, NY 10019
Attention: Russ Leaf; Jared Fertman
Email: rleaf@willkie.com; jfertman@willkie.com

Any notice or communication sent to a Holder of Physical Notes shall be mailed to it by first class mail, postage prepaid, at its address as it appears on the Note Register and shall be sufficiently given to it if so mailed within the time prescribed Any notice or communication sent to Holders of Global Notes shall be sent in accordance with the applicable procedures of the Depositary and shall be sufficiently given to it if so sent within the time prescribed.

Failure to deliver a notice or communication to a Holder or any defect in it shall not affect its sufficiency with respect to other Holders. If a notice or communication is sent or delivered in the manner provided above, it is duly given, whether or not the addressee receives it.

In case by reason of the suspension of regular mail service or by reason of any other cause it shall be impracticable to give such notice to Holders by mail, then such notification as shall be made with the approval of the Trustee shall constitute a sufficient notification for every purpose hereunder.

In addition to the foregoing, the Trustee agrees to accept and act upon notice, instructions or directions pursuant to this Indenture sent by unsecured e-mail, facsimile transmission or other

similar unsecured electronic methods. If the party elects to give the Trustee e-mail or facsimile instructions (or instructions by a similar electronic method), and the Trustee acts upon such instructions, the Trustee's understanding of such instructions shall be deemed controlling. The Trustee shall not be liable for any losses, costs or expenses arising directly or indirectly from the Trustee's reliance upon and compliance with such instructions notwithstanding such instructions conflict or are inconsistent with a subsequent written instruction. The party providing electronic instructions agrees to assume all risks arising out of the use of such electronic methods to submit instructions and directions to the Trustee, including the risk of the Trustee acting on unauthorized instructions, and the risk or interception and misuse by third parties.

Section 15.04. *Governing Law; Jurisdiction.* THIS INDENTURE, THE GUARANTEE AND EACH NOTE, AND ANY CLAIM, CONTROVERSY OR DISPUTE ARISING UNDER OR RELATED TO THIS INDENTURE, THE GUARANTEE AND EACH NOTE, SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH, THE LAWS OF THE STATE OF NEW YORK.

Each of the Company and the Guarantors irrevocably consents and agrees, for the benefit of the Holders from time to time of the Notes, the Holders' Representative and the Trustee, that any legal action, suit or proceeding against it with respect to obligations, liabilities or any other matter arising out of or in connection with this Indenture, the Guarantee or the Notes may be brought in the courts of the State of New York or the courts of the United States located in the Borough of Manhattan, New York City, New York and, until amounts due and to become due in respect of the Notes have been paid, hereby irrevocably consents and submits to the non-exclusive jurisdiction of each such court *in personam*, generally and unconditionally with respect to any action, suit or proceeding for itself in respect of its properties, assets and revenues.

Each of the Company and the Guarantors irrevocably and unconditionally waives, to the fullest extent permitted by law, any objection which it may now or hereafter have to the laying of venue of any of the aforesaid actions, suits or proceedings arising out of or in connection with this Indenture, the Notes or the Guarantee brought in the courts of the State of New York or the courts of the United States located in the Borough of Manhattan, New York City, New York and hereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum.

Section 15.05. *Evidence of Compliance with Conditions Precedent; Certificates and Opinions of Counsel to Trustee.* Upon any application or demand by the Company or any Guarantor to the Trustee to take any action under any of the provisions of this Indenture, the Company or such Guarantor, as applicable, shall furnish to the Trustee an Officer's Certificate and/or Opinion of Counsel, subject to customary exceptions, in form and substance reasonably satisfactory to the Trustee, stating that such action is permitted by the terms of the Indenture and that all conditions precedent, if any, provided for in this Indenture relating to the proposed action have been complied with.

Each Officer's Certificate or Opinion of Counsel provided for in this Indenture and delivered to the Trustee with respect to compliance with a condition or covenant provided for in this Indenture shall include (a) a statement that the person signing such Officer's Certificate or Opinion of Counsel has read such covenant or condition, (b) a brief statement as to the nature and scope of the examination or investigation upon which the statements or opinions contained in such Officer's Certificate or Opinion of Counsel are based, (c) a statement that, in the opinion of such person, he or she has made such examination or investigation as is necessary to enable him or her to express an informed opinion as to whether or not such action is permitted by this Indenture and whether or not such covenants or conditions have been complied with and (d) a statement as to whether or not, in the opinion of such person, such action is permitted by this Indenture and that all conditions or covenants precedent to such action have been complied with.

Any Officer's Certificate of the Company or any Guarantor may be based, insofar as it relates to legal matters, upon an Opinion of Counsel, unless such officer knows that the Opinion of Counsel with respect to the matters upon which his or her Officer's Certificate may be based as aforesaid are erroneous, or in the exercise of reasonable care should know that the same are erroneous. Any Opinion of Counsel may be based, insofar as it relates to factual matters, information with respect to which is in the possession of the Company or any Guarantor, upon the Officer's Certificate of the Company or such Guarantor, as applicable, unless such counsel knows that the Officer's Certificate with respect to the matters upon which his or her Opinion of Counsel may be based as aforesaid are erroneous, or in the exercise of reasonable care should know that the same are erroneous.

Any Officer's Certificate or Opinion of Counsel may be based, insofar as it relates to accounting matters, upon a certificate or opinion of or representations by an accountant or firm of accountants in the employ of the Company or any Guarantor, as applicable, unless such officer or counsel, as the case may be, knows that the certificate or opinion or representations with respect to the accounting matters upon which his or her Officer's Certificate or Opinion of Counsel may be based as aforesaid are erroneous, or in the exercise of reasonable care should know that the same are erroneous.

Any certificate or opinion of any independent firm of public accountants filed with and directed to the Trustee shall contain a statement that such firm is independent.

Section 15.06. *Legal Holidays.* In any case where any Payment Date is not a Business Day, then any action to be taken on such date need not be taken on such date, but may be taken on the next succeeding Business Day with the same force and effect as if taken on such date, and no interest shall accrue in respect of the delay.

Section 15.07. *No Security Interest Created.* Nothing in this Indenture or in the Notes, expressed or implied, shall be construed to constitute a security interest under the Uniform Commercial Code or similar legislation, as now or hereafter enacted and in effect, in any jurisdiction.

Section 15.08. *Benefits of Indenture.* Nothing in this Indenture or in the Notes, expressed or implied, shall give to any Person, other than the Holders, the parties hereto, the holders of Senior Debt, any Paying Agent, any authenticating agent, any Note Registrar and their successors hereunder, any benefit or any legal or equitable right, remedy or claim under this Indenture.

Section 15.09. *Table of Contents, Headings, Etc.* The table of contents and the titles and headings of the articles and sections of this Indenture have been inserted for convenience of reference only, are not to be considered a part hereof, and shall in no way modify or restrict any of the terms or provisions hereof.

Section 15.10. *Authenticating Agent.* The Trustee may appoint an authenticating agent that shall be authorized to act on its behalf and subject to its direction in the authentication and delivery of Notes in connection with the original issuance thereof and transfers and exchanges of Notes hereunder, including under Section 2.04, Section 2.05, Section 2.06, Section 2.07 and Section 10.04 as fully to all intents and purposes as though the authenticating agent had been expressly authorized by this Indenture and those Sections to authenticate and deliver Notes. For all purposes of this Indenture, the authentication and delivery of Notes by the authenticating agent shall be deemed to be authentication and delivery of such Notes "by the Trustee" and a certificate of authentication executed on behalf of the Trustee by an authenticating agent shall be deemed to satisfy any requirement hereunder or in the Notes for the Trustee's certificate of authentication. Such authenticating agent shall at all times be a Person eligible to serve as trustee hereunder pursuant to Section 7.08.

Any corporation or other entity into which any authenticating agent may be merged or converted or with which it may be consolidated, or any corporation or other entity resulting from any merger, consolidation or conversion to which any authenticating agent shall be a party, or any corporation or other entity succeeding to the corporate trust business of any authenticating agent, shall be the successor of the authenticating agent hereunder, if such successor corporation or other entity is otherwise eligible under this Section 15.10, without the execution or filing of any paper or any further act on the part of the parties hereto or the authenticating agent or such successor corporation or other entity.

Any authenticating agent may at any time resign by giving written notice of resignation to the Trustee and to the Company. The Trustee may at any time terminate the agency of any authenticating agent by giving written notice of termination to such authenticating agent and to the Company. Upon receiving such a notice of resignation or upon such a termination, or in case at any time any authenticating agent shall cease to be eligible under this Section, the Trustee may appoint a successor authenticating agent (which may be the Trustee), shall give written notice of such appointment to the Company and shall send notice of such appointment to all Holders as the names and addresses of such Holders appear on the Note Register.

The Company agrees to pay to the authenticating agent from time to time reasonable compensation for its services although the Company may terminate the authenticating agent, if it determines such agent's fees to be unreasonable.

The provisions of Section 7.02, Section 7.03, Section 7.04, Section 8.03 and this Section 15.10 shall be applicable to any authenticating agent.

If an authenticating agent is appointed pursuant to this Section 15.10, the Notes may have endorsed thereon, in addition to the Trustee's certificate of authentication, an alternative certificate of authentication in the following form:

_____,
as Authenticating Agent, certifies that this is one of the Notes described
in the within-named Indenture.

By: _____
Authorized Signatory

Section 15.11. *Execution in Counterparts.* This Indenture may be executed in any number of counterparts, each of which shall be an original, but such counterparts shall together constitute but one and the same instrument. The exchange of copies of this Indenture and of signature pages by facsimile or PDF transmission shall constitute effective execution and delivery of this Indenture as to the parties hereto and may be used in lieu of the original Indenture for all purposes. Signatures of the parties hereto transmitted by facsimile or PDF shall be deemed to be their original signatures for all purposes.

Section 15.12. *Conflict with Trust Indenture Act.* If any provision hereof limits, qualifies or conflicts with another provision hereof which is required to be included in this Indenture by any of the provisions of the Trust Indenture Act, such required provision shall control.

Section 15.13. *Severability.* In the event any provision of this Indenture or in the Notes shall be invalid, illegal or unenforceable, then (to the extent permitted by law) the validity, legality or enforceability of the remaining provisions shall not in any way be affected or impaired.

Section 15.14. *Waiver of Jury Trial.* EACH OF THE COMPANY, THE GUARANTORS, THE HOLDERS' REPRESENTATIVE AND THE TRUSTEE HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS INDENTURE, THE GUARANTEE, THE NOTES OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THEREBY.

Section 15.15. *Force Majeure.* In no event shall the Trustee be responsible or liable for any failure or delay in the performance of its obligations hereunder arising out of or caused by, directly or indirectly, forces beyond its control, including strikes, work stoppages, accidents, acts

of war or terrorism, civil or military disturbances, nuclear or natural catastrophes or acts of God, and interruptions, loss or malfunctions of utilities, communications or computer (software and hardware) services; it being understood that the Trustee shall use reasonable efforts that are consistent with accepted practices in the banking industry to resume performance as soon as practicable under the circumstances.

Section 15.16. *Calculations*. Except as otherwise provided herein (including Section 9.10), the Company shall be responsible for making all calculations called for under the Notes. These calculations include, but are not limited to, determinations of any accrued Default Interest payable on the Notes. The Company shall make all these calculations in good faith and, absent manifest error, the Company's calculations shall be final and binding on Holders of Notes; provided, that the foregoing shall not apply with respect to the determination as to whether Default Interest is due. The Company shall provide a schedule of its calculations to the Trustee, and the Trustee is entitled to rely conclusively upon the accuracy of the Company's calculations without independent verification. The Trustee will forward the Company's calculations to any Holder of Notes upon the request of that Holder at the sole cost and expense of the Company. The Trustee shall have no obligations under this Indenture to monitor, verify or perform any calculations under this Indenture or the Notes.

Section 15.17. *U.S.A. Patriot Act.* The parties hereto acknowledge that in accordance with Section 326 of the U.S.A. Patriot Act, the Trustee (in all of its capacities), like all financial institutions and in order to help fight the funding of terrorism and money laundering, is required to obtain, verify, and record information that identifies each person or legal entity that establishes a relationship or opens an account with the Trustee. The parties to this Indenture agree that they will provide the Trustee with such information as it may request in order for the Trustee to satisfy the requirements of the U.S.A. Patriot Act.

Section 15.18. *Tax Withholding.* The Company or the Trustee, as the case may be, shall be entitled to make a deduction or withholding from any payment which it makes under this Indenture for or on account of any present or future taxes, duties or charges if and to the extent so required by any applicable law and any current or future regulations or agreements thereunder or official interpretations thereof or any law implementing an intergovernmental approach thereto or by virtue of the relevant Holder failing to satisfy any certification or other requirements in respect of the Notes, in which event the Company or the Trustee, as the case may be, shall make such payment after such withholding or deduction has been made and shall account to the relevant authorities for the amount so withheld or deducted and shall have no obligation to gross up any payment hereunder or pay any additional amount as a result of such withholding tax.

ARTICLE 16
SUBORDINATION OF NOTES

Section 16.01. *Notes Subordinate to Senior Debt.* The Company covenants and agrees, and each Holder of a Note, whether upon original issue or upon transfer, assignment or exchange

thereof, by such Holder's acceptance thereof, likewise covenants and agrees, that, notwithstanding anything in this Indenture or the Notes to the contrary, the indebtedness evidenced by the Notes and the payment of the principal of (and premium, if any) and interest on each and all of the Notes are hereby expressly made subordinate and junior in right of payment to the prior payment in full in cash of all Senior Debt, whether outstanding at the date of this Indenture or thereafter incurred, to the extent and in the manner provided in this Indenture.

Section 16.02. *Payment Over of Proceeds Upon Dissolution, Etc.* In the event of (a) any insolvency or bankruptcy case or proceeding, or any receivership, liquidation, reorganization or other similar case or proceeding in connection therewith, relative to the Company, any Guarantor or to their respective creditors, as such, or to their respective assets, or (b) any liquidation, dissolution or other winding up of the Company or any Guarantor, whether voluntary or involuntary and whether or not involving insolvency or bankruptcy, or (c) any assignment for the benefit of creditors or any other marshalling of assets and liabilities of the Company or any Guarantor, then and in any such event the holders of Senior Debt shall be entitled to receive payment in full of all amounts due or to become due on or in respect of all Senior Debt (including any interest accruing thereon after the commencement of any such case or proceeding), or provision shall be made for such payment in cash or cash equivalents or otherwise in a manner satisfactory to the holders of Senior Debt, before the Holders of the Notes are entitled to receive any payment on account of principal of (or premium, if any) or interest on the Notes, and to that end the holders of Senior Debt shall be entitled to receive, for application to the payment thereof, any payment or distribution of any kind or character, whether in cash, property or securities, including any such payment or distribution which may be payable or deliverable by reason of the payment of any other indebtedness of the Company or any Guarantor being subordinated to the payment of the Notes, which may be payable or deliverable in respect of the Notes in any such case, proceeding, dissolution, liquidation or other winding up event.

In the event that, notwithstanding the foregoing provisions of this Section, the Trustee or the Holder of any Note shall have received any payment or distribution of assets of the Company or any Guarantor of any kind or character, whether in cash, property or securities, including any such payment or distribution which may be payable or deliverable by reason of the payment of any other indebtedness of the Company or any Guarantor being subordinated to the payment of the Notes, before all Senior Debt is paid in full or payment thereof provided for, and if such fact shall, at or prior to the time of such payment or distribution, have been made known to the Trustee or, as the case may be, such Holder, then and in such event such payment or distribution shall be paid over or delivered forthwith to the trustee in bankruptcy, receiver, liquidating trustee, custodian, assignee, agent or other Person making payment or distribution of assets of the Company or any Guarantor for application to the payment of all Senior Debt remaining unpaid, to the extent necessary to pay all Senior Debt in full, after giving effect to any concurrent payment or distribution to or for the holders of Senior Debt. Any taxes that have been withheld or deducted from any payment or distribution in respect of the Notes, or any taxes that ought to have been withheld or deducted from any such payment or distribution that have been remitted to

the relevant taxing authority, shall not be considered to be an amount that the Trustee or the Holder of any Note receives for purposes of this Section.

For purposes of this Article only, the words "cash, property or securities" shall not be deemed to include shares of stock of the Company as reorganized or readjusted, or securities of the Company or any other corporation or other entity, provided for by a plan of reorganization or readjustment which are subordinated in right of payment to all Senior Debt which may at the time be outstanding to substantially the same extent as, or to a greater extent than, the Notes are so subordinated as provided in this Article.

Section 16.03. *No Payment When Senior Debt in Default*. In the event and during the continuation of any default in the payment of principal of (or premium, if any), interest or other amounts due on any Senior Debt beyond any applicable grace period with respect thereto, or in the event that any event of default with respect to any Senior Debt shall have occurred and be continuing permitting the holders of such Senior Debt (or a trustee on behalf of the holders thereof) to declare such Senior Debt due and payable prior to the date on which it would otherwise have become due and payable, unless and until such event of default shall have been waived in writing and any such declaration and its consequences shall have been rescinded or annulled, or in the event that any judicial proceeding shall be pending with respect to any such default in payment or event of default, or in the event that any event of default with respect to any Senior Debt would result from any payments of the Notes, then no payments (including Principal Payments, Interest Payments, payments of Default Interest, or to the extent applicable, any payment which may be payable by reason of the payment of any other indebtedness of the Company being subordinated to the payment of the Note) shall be made by the Company or any Guarantor on the Notes or on account of the purchase or other acquisition of Notes.

In the event that, notwithstanding the foregoing, the Company or any Guarantor shall make any payment to the Trustee or the Holder of any Note prohibited by the provisions of this Section, and if such fact shall, at or prior to the time of such payment, have been made known to the Trustee or, as the case may be, such Holder, then and in such event such payment shall be paid over and delivered to the Company for application to the payment of all Senior Debt remaining unpaid, to the extent necessary to pay all Senior Debt in full, after giving effect to any concurrent payment or distribution to or for the holders of Senior Debt. The provisions of this Section shall not apply to any payment with respect to which Section 16.02 would be applicable.

Section 16.04. *Payment Permitted in Certain Situations*. Nothing contained in this Article or elsewhere in this Indenture or in any of the Notes shall prevent, at any time except during the pendency of any case, proceeding, dissolution, liquidation or other winding up, assignment for the benefit of creditors or other marshalling of assets and liabilities of the Company or any Guarantor referred to in Section 16.02 or under the conditions described in Section 16.03, (a) the Company from making Principal Payments, Interest Payments or payments of Default Interest at any time on the Notes, or on account of the purchase or other acquisition of Notes, including pursuant to any Optional Redemption in accordance with Article 14, or (b) the application by the Trustee of any money deposited with it hereunder to any Principal Payment,

Interest Payment or payment of Default Interest on the Notes or the retention of such payment by the Holders, if, at the time of such application by the Trustee, it did not have knowledge that such payment would have been prohibited by the provisions of this Article.

Section 16.05. *Subrogation to Rights of Holders of Senior Debt.* Subject to the payment in full of all Senior Debt or the provision for such payment in cash or cash equivalents or otherwise in a manner satisfactory to the holders of Senior Debt, the Holders of the Notes shall be subrogated to the extent of the payments or distributions made to the holders of such Senior Debt pursuant to the provisions of this Article (equally and ratably with the holders of indebtedness of the Company which by its express terms is subordinated to indebtedness of the Company to substantially the same extent as the Notes are subordinated to the Senior Debt and is entitled to like rights of subrogation) to the rights of the holders of such Senior Debt to receive payments and distributions of cash, property and securities applicable to the Senior Debt to the extent that Principal Payments, Interest Payments or payments of Default Interest are payable under this Indenture and the Notes. For purposes of such subrogation, no payments or distributions to the holders of the Senior Debt of any cash, property or securities to which the Holders of the Notes or the Trustee would be entitled except for the provisions of this Article, and no payments over pursuant to the provisions of this Article to the holders of Senior Debt by Holders of the Notes or the Trustee, shall, as among the Company, its creditors other than holders of Senior Debt and the Holders of the Notes, be deemed to be a payment or distribution by the Company to or on account of the Senior Debt.

Section 16.06. *Provisions Solely to Define Relative Rights.* The provisions of this Article are and are intended solely for the purpose of defining the relative rights of the Holders of the Notes on the one hand and the holders of Senior Debt on the other hand. Nothing contained in this Article 16 is intended to or shall (i) impair, as between the Company and the Holders of the Notes, the obligation of the Company to pay to the Holders of the Notes the principal of (and premium, if any) and interest on the Notes as and when the same shall become due and payable in accordance with their terms or prevent the Trustee or the Holder of any Note from exercising all remedies otherwise permitted by applicable law upon default under this Indenture, subject to the rights of the holders of Senior Debt to receive cash, property and securities otherwise payable or deliverable to the Trustee or such Holder in accordance with this Article 16, (ii) enhance the rights of the Holders of the Notes to the Principal Payments, Interest Payments and payments of Default Interest payable on the Notes in accordance with their terms, or (iii) cause any additional Principal Payments, Interest Payments or Default Interest, or other amounts, to be due and payable to the Holders of the Notes.

Section 16.07. *Trustee to Effectuate Subordination*. Each Holder of a Note by such Holder's acceptance thereof authorizes and directs the Trustee on such Holder's behalf to take such action as may be necessary or appropriate to effectuate the subordination provided in this Article and appoints the Trustee as such Holder's attorney-in-fact for any and all such purposes.

Section 16.08. *No Waiver of Subordination Provisions*. No right of any present or future holder of any Senior Debt to enforce subordination as herein provided shall at any time in any

way be prejudiced or impaired by any act or failure to act on the part of the Company or any Guarantor or by any act or failure to act, in good faith, by any such holder, or by any non-compliance by the Company or any Guarantor with the terms, provisions and covenants of this Indenture, regardless of any knowledge thereof any such holder may have or be otherwise charged with. Without in any way limiting the generality of the foregoing paragraph, the holders of Senior Debt may, at any time and from time to time, and in their absolute discretion, change the manner, place or terms of payment or extend the time of payment of, or renew or alter, any such Senior Debt or otherwise amend or supplement in any manner such Senior Debt or any instrument evidencing the same or any agreement under which such Senior Debt is outstanding.

Section 16.09. *Notice to Trustee*. The Company shall give prompt written notice to the Trustee of any fact known to the Company which would prohibit the making of any payment to or by the Trustee in respect of the Notes. Notwithstanding the provisions of this Article or any other provision of this Indenture, the Trustee shall not be charged with knowledge of the existence of any facts which would prohibit the making of any payment to or by the Trustee in respect of the Notes, unless and until the Trustee shall have received written notice thereof from the Company or a holder of Senior Debt or from any trustee therefor; and, prior to the receipt of any such written notice, the Trustee, subject to the provisions of Section 7.01, shall be entitled in all respects to assume that no such facts exist; provided, however, that if on a date at least two Business Days prior to the date upon which by the terms hereof any such moneys shall become payable for any purpose (including the payment of the principal of, or interest on any Notes) the Trustee shall not have received with respect to such moneys the notice provided for in this Section 16.09, but subsequently receives such notice prior to applying such funds (including the payment of the principal of, or interest on any Notes) and the Trustee is unable to administratively stop such application of funds to the Holders, then, the Trustee shall not be deemed in breach of this Indenture for applying such funds as long as the Trustee immediately, upon receipt of such notice, notifies the Holders of the facts prohibiting the such application of funds, that such application funds should not have been made and that such funds are required to be returned in accordance with the terms of this Indenture, and the Trustee shall provide commercially reasonable assistance necessary to facilitate the return of such funds to the holder of Senior Debt in accordance with the terms of this Indenture. Subject to the provisions of Section 7.01, the Trustee shall be entitled to rely on the delivery to it of a written notice by a Person representing himself to be a holder of Senior Debt (or a trustee therefor) to establish that such notice has been given by a holder of Senior Debt (or a trustee therefor). In the event that the Trustee determines in good faith that further evidence is required with respect to the right of any Person as a holder of Senior Debt to participate in any payment or distribution pursuant to this Article, the Trustee may request such Person to furnish evidence to the reasonable satisfaction of the Trustee as to the amount of Senior Debt held by such Person, the extent to which such Person is entitled to participate in such payment or distribution and any other facts pertinent to the rights of such Person under this Article, and if such evidence is not furnished, the Trustee may defer any payment to such Person pending judicial determination as to the right of such Person to receive such payment.

Section 16.10. *Reliance on Judicial Order or Certificate of Liquidating Agent.* Upon any payment or distribution of assets of the Company or any Guarantor referred to in this Article, the Trustee, subject to the provisions of Section 7.01, and the Holders of the Notes shall be entitled to rely upon any order or decree entered by any court of competent jurisdiction in which such insolvency, bankruptcy, receivership, liquidation, reorganization, dissolution, winding up or similar case or proceeding is pending, or a certificate of the trustee in bankruptcy, receiver, liquidating trustee, custodian, assignee for the benefit of creditors, agent or other Person making such payment or distribution, delivered to the Trustee or to the Holders of Notes, for the purpose of ascertaining the Persons entitled to participate in such payment or distribution, the holders of Senior Debt and other indebtedness of the Company, the amount thereof or payable thereon, the amount or amounts paid or distributed thereon and all other facts pertinent thereto or to this Article.

Section 16.11. *Trustee Not Fiduciary for Holders of Senior Debt*. The Trustee shall not be deemed to owe any fiduciary duty to the holders of Senior Debt and shall not be liable to any such holders or creditors if it shall in good faith pay over or distribute to Holders of Notes or to the Company or to any other Person cash, property or securities to which any holders of Senior Debt shall be entitled by virtue of this Article or otherwise. With respect to the holders of Senior Debt, the Trustee undertakes to perform or to observe only such of its covenants or obligations as are specifically set forth in this Article and no implied covenants or obligations with respect to holders of Senior Debt shall be read into this Indenture against the Trustee.

Section 16.12. *Rights of Trustee as Holder of Senior Debt; Preservation of Trustee's Rights.* The Trustee in its individual capacity shall be entitled to all the rights set forth in this Article with respect to any Senior Debt which may at any time be held by it, to the same extent as any other holder of Senior Debt and nothing in this Indenture shall deprive the Trustee of any of its rights as such holder. Nothing in this Article shall apply to claims of, or payments to, the Trustee under or pursuant to Section 7.06.

Section 16.13. *Article Applicable to Paying Agents.* In case at any time any Paying Agent other than the Trustee shall have been appointed by the Company and be then acting hereunder, the term "Trustee" as used in this Article shall in such case (unless the context otherwise requires) be construed as extending to and including such Paying Agent within its meaning as fully for all intents and purposes as if such Paying Agent were named in this Article in addition to or in place of the Trustee.

Section 16.14. *Modification of Subordination Provisions*. Anything in Article 16 or elsewhere contained in this Indenture to the contrary notwithstanding, no modification or amendment of this Indenture and no supplemental indenture shall modify the subordination provisions of this Article 16 in a manner that would adversely affect the holders of Senior Debt.

Section 16.15. *Senior Debt Entitled to Rely.* Each holder of a Note, by accepting such Note, acknowledges and agrees that the subordination provisions contained in this Article 16 are, and are intended to be, an inducement and a consideration to each holder of the Senior Debt,

whether the Senior Debt was created or acquired before or after the issuance of the Notes, to acquire or continue to hold the Senior Debt, and such holders of the Senior Debt shall have the right to rely upon this Article 16, and no amendment or modification of the provisions contained herein shall diminish the rights of such holders unless such holders shall have agreed in writing thereto. Each holder of a Note, by accepting such Note, and the Trustee, on behalf of the holders of such Notes, hereby waives the benefits, if any, of any statutory or common law rule that may permit a subordinating creditor to assert any defenses of a surety or guarantor, or that may give the subordinating creditor the right to require a senior creditor to marshal assets, and they each agree that it shall not assert any such defenses or rights.

Section 16.16. *Reinstatement.* To the extent the payment of or distribution in respect of the Senior Debt (whether by or on behalf of the Company as proceeds of security or enforcement of any right of setoff or otherwise) is declared to be fraudulent or preferential, set aside or required to be paid to any receiver, trustee in bankruptcy, liquidating trustee, agent or similar Person under any bankruptcy, insolvency, receivership, fraudulent conveyance or similar law, then if such payment or distribution is recovered by, or paid over to, such receiver, trustee in bankruptcy, liquidating trustee, agent or similar Person, the Senior Debt or part thereof originally intended to be satisfied shall be deemed to be reinstated and outstanding as if such payment had not occurred.

Section 16.17. *Action by Holders of Senior Debt.* The holders of the Senior Debt may, at any time and from time to time, without the consent of or notice to the Trustee or the Holders, without incurring responsibility to the Holders and without impairing or releasing the subordination provided in this Indenture or the obligations of the Holders hereunder to the holders of the Senior Debt, take any action deemed appropriate in the sole discretion of the holders of Senior Debt, including, without limitation, doing any one or more of the following:

(i) change the manner, place or terms of payment or extend the time of payment of, or renew or alter, the Senior Debt or any instrument evidencing the same or any agreement under which the Senior Debt is outstanding or secured;

(ii) sell, exchange, release or otherwise deal with any property pledged, mortgaged or otherwise secured;

(iii) release any Person liable in any manner for the collection of the Senior Debt;

(iv) exercise or refrain from exercising any rights against the Company or any other Person; and

(v) take any other action in the reasonable business judgment of the holders of the Senior Debt.

No such action or inaction shall impair or otherwise affect the holder of the Senior Debt's rights under the Notes or this Indenture.

[Remainder of page intentionally left blank]

IN WITNESS WHEREOF, the parties hereto have caused this Indenture to be duly executed as of the date first written above.

ITERUM THERAPEUTICS BERMUDA LIMITED, as Notes Issuer

By: /s/ Louise Barrett
Name:Louise Barrett
Title: Director

ITERUM THERAPEUTICS PLC, as Guarantor

By: /s/ David Kelly
Name: David Kelly
Title: Director

ITERUM THERAPEUTICS INTERNATIONAL LIMITED, as Guarantor

By: /s/ Louise Barrett
Name: Louise Barrett
Title: Director

ITERUM THERAPEUTICS U.S. LIMITED, as Guarantor

By: /s/ Judith M. Matthews
Name: Judith M. Matthews
Title: Director

ITERUM THERAPEUTICS U.S. HOLDING Limited, as Guarantor

By: /s/ Judith M. Matthews
Name: Judith M. Matthews
Title: Director

Iterum Holders' Representative LLC, as Holders' Representative

By: /s/ Patrice Bonfiglio

Name:Patrice Bonfiglio

Title: Chief Financial Officer

COMPUTERSHARE TRUST COMPANY, N.A., as Trustee

By: /s/ Jerry Urbanek

Name: Jerry Urbanek

Title: Trust Officer

EXHIBIT A

Form of Note

[FORM OF FACE OF NOTE]

[THIS NOTE AND THE INDEBTEDNESS EVIDENCED HEREBY ARE, TO THE EXTENT PROVIDED IN THE INDENTURE PURSUANT TO WHICH THIS NOTE IS ISSUED, SUBORDINATE AND SUBJECT IN RIGHT OF PAYMENT TO THE PRIOR PAYMENT IN FULL OF ALL SENIOR DEBT, AND THIS NOTE IS ISSUED SUBJECT TO THE PROVISIONS OF THE INDENTURE WITH RESPECT THERETO. BY ITS ACCEPTANCE HEREOF, EACH HOLDER AND ANY BENEFICIAL OWNER OF THIS NOTE IRREVOCABLY (A) AGREES TO BE BOUND BY SUCH PROVISIONS OF THE INDENTURE, (B) AUTHORIZES AND DIRECTS THE TRUSTEE ON HIS, HER OR ITS BEHALF TO TAKE SUCH ACTIONS AS MAY BE NECESSARY OR APPROPRIATE TO EFFECTUATE THE SUBORDINATION SO PROVIDED, (C) APPOINTS THE TRUSTEE AS HIS, HER OR ITS ATTORNEY-IN-FACT FOR ANY AND ALL SUCH PURPOSES AND (D) WAIVES ALL NOTICE OF THE ACCEPTANCE OF THE SUBORDINATION PROVISIONS CONTAINED HEREIN AND IN THE INDENTURE BY EACH HOLDER OF SENIOR DEBT, WHETHER NOW OUTSTANDING OR HEREAFTER CREATED, INCURRED, ASSUMED OR GUARANTEED, AND WAIVES RELIANCE BY EACH SUCH HOLDER UPON SAID PROVISIONS.]

[INCLUDE FOLLOWING LEGEND IF A GLOBAL NOTE]

[UNLESS THIS CERTIFICATE IS PRESENTED BY AN AUTHORIZED REPRESENTATIVE OF THE DEPOSITORY TRUST COMPANY, A NEW YORK CORPORATION ("DTC"), TO THE COMPANY OR ITS AGENT FOR REGISTRATION OF TRANSFER, EXCHANGE, OR PAYMENT, AND ANY CERTIFICATE ISSUED IS REGISTERED IN THE NAME OF CEDE & CO. OR IN SUCH OTHER NAME AS IS REQUESTED BY AN AUTHORIZED REPRESENTATIVE OF DTC (AND ANY PAYMENT HEREUNDER IS MADE TO CEDE & CO. OR TO SUCH OTHER ENTITY AS IS REQUESTED BY AN AUTHORIZED REPRESENTATIVE OF DTC), ANY TRANSFER, PLEDGE, OR OTHER USE HEREOF FOR VALUE OR OTHERWISE BY OR TO ANY PERSON IS WRONGFUL INASMUCH AS THE REGISTERED OWNER HEREOF, CEDE & CO., HAS AN INTEREST HEREIN.]

[INCLUDE FOLLOWING LEGEND IF A RESTRICTED SECURITY]

[THIS SECURITY HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), AND MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED EXCEPT IN ACCORDANCE WITH THE FOLLOWING SENTENCE. BY ITS ACQUISITION HEREOF OR OF A BENEFICIAL INTEREST HEREIN, THE ACQUIRER:

(1) REPRESENTS THAT IT AND ANY ACCOUNT FOR WHICH IT IS ACTING IS A "ACCREDITED INVESTOR" (WITHIN THE MEANING OF RULE 501 UNDER THE SECURITIES ACT) AND THAT IT EXERCISES SOLE INVESTMENT DISCRETION WITH RESPECT TO EACH SUCH ACCOUNT, AND THAT IT AND ANY SUCH ACCOUNT IS NOT AN AFFILIATE OF ITERUM THERAPEUTICS BERMUDA LIMITED (THE "COMPANY"), ITERUM THERAPEUTICS PLC (THE "PARENT GUARANTOR"), ITERUM THERAPEUTICS INTERNATIONAL LIMITED (THE "IRISH GUARANTOR"), ITERUM THERAPEUTICS US LIMITED ("ITERUM U.S. LIMITED") OR ITERUM THERAPEUTICS US HOLDING LIMITED (TOGETHER WITH ITERUM, THE IRISH GUARANTOR AND ITERUM U.S. LIMITED, THE "GUARANTORS"), AND

(2) AGREES FOR THE BENEFIT OF THE COMPANY AND THE GUARANTORS THAT IT WILL NOT OFFER, SELL, PLEDGE OR OTHERWISE TRANSFER THIS SECURITY OR ANY BENEFICIAL INTEREST HEREIN PRIOR TO THE DATE THAT IS THE LATER OF (X) ONE YEAR AFTER THE LAST ORIGINAL ISSUE DATE HEREOF OR SUCH SHORTER PERIOD OF TIME AS PERMITTED BY RULE 144 UNDER THE SECURITIES ACT OR ANY SUCCESSOR PROVISION THERETO AND (Y) SUCH LATER DATE, IF ANY, AS MAY BE REQUIRED BY APPLICABLE LAW, EXCEPT:

(A) TO ANY GUARANTOR OR ANY SUBSIDIARY THEREOF (INCLUDING THE COMPANY), OR

(B) PURSUANT TO A REGISTRATION STATEMENT WHICH HAS BECOME EFFECTIVE UNDER THE SECURITIES ACT, OR

(C) TO A QUALIFIED INSTITUTIONAL BUYER IN COMPLIANCE WITH RULE 144A UNDER THE SECURITIES ACT, OR

(D) PURSUANT TO AN EXEMPTION FROM REGISTRATION PROVIDED BY RULE 144 UNDER THE SECURITIES ACT (IF AVAILABLE) OR ANY OTHER AVAILABLE EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

PRIOR TO THE REGISTRATION OF ANY TRANSFER IN ACCORDANCE WITH CLAUSE (2)(D) ABOVE, THE COMPANY, THE GUARANTORS AND THE TRUSTEE RESERVE THE RIGHT TO REQUIRE THE DELIVERY OF SUCH LEGAL OPINIONS, CERTIFICATIONS OR OTHER EVIDENCE AS MAY REASONABLY BE REQUIRED IN ORDER TO DETERMINE THAT THE PROPOSED TRANSFER IS BEING MADE IN COMPLIANCE WITH THE SECURITIES ACT AND APPLICABLE STATE SECURITIES LAWS. NO REPRESENTATION IS MADE AS TO THE AVAILABILITY OF ANY EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

THE HOLDER OF THIS SECURITY IS ENTITLED TO THE BENEFITS OF AN INVESTOR RIGHTS AGREEMENT (AS SUCH TERM IS DEFINED IN THE INDENTURE REFERRED TO ON THE REVERSE HEREOF) AND, BY ITS ACCEPTANCE HEREOF, AGREES TO BE BOUND BY AND TO COMPLY WITH THE PROVISIONS OF SUCH INVESTOR RIGHTS AGREEMENT.]

Iterum Therapeutics Bermuda Limited

Limited Recourse Royalty-Linked Subordinated Note

Certificate No. [_____] [Initially][1] $[_____]

CUSIP No. [ ]

[ISIN No. [•]]

Iterum Therapeutics Bermuda Limited, a company formed under the laws of Bermuda (the "**Company**," which term includes any successor corporation or other entity under the Indenture referred to on the reverse hereof), for value received hereby promises to pay to [CEDE & CO.][2] [_____][3], or registered assigns, the Principal Amount [as set forth in the "Schedule of Exchanges of Notes" attached hereto][4] [of $[_____]][5] provided that (a) the Principal Amount, taken together with the Principal Amounts in respect of all other Notes, shall not initially exceed $120,000 in aggregate at any time, (b) the Principal Payments and Interest Payments, taken together with the Principal Payments and Interest Payments in respect of all other Notes, shall not exceed $480,000,000 in the aggregate, and (c) the Principal Payments and Interest Payments shall in all events be payable on the terms and subject to the conditions, including the End Date, the Maximum Return Amount Qualification and the Limited Recourse Qualification, set forth in this Note and in the Indenture. This Note is fully and unconditionally guaranteed by Iterum Therapeutics plc, a company formed under the laws of Ireland (the "**Parent Guarantor**"), Iterum Therapeutics International Limited, a company formed under the laws of Ireland (the "**Irish Guarantor**"), Iterum Therapeutics US Limited, a Delaware corporation ("**Iterum U.S. Limited**") and Iterum Therapeutics US Holding Limited, a Delaware corporation ("**Iterum U.S. Holding**" and, together with Parent Guarantor, the Irish Guarantor and Iterum U.S. Limited, the "**Guarantors**"), on a senior unsecured basis, in accordance with the provisions of Article 13 of the Indenture. Notwithstanding anything in this Note to the contrary, the guarantee of the Note by the Guarantors is subordinate in right of payment to any Guarantor Senior Debt to the extent and in the manner provided in the Indenture, and by its acceptance hereof, each Holder and any beneficial owner of this Note irrevocably agrees to be bound by such provisions of the Indenture.

Any Defaulted Amounts shall accrue Default Interest at a per annum rate equal, as of any date that Default Interest accrues, to the prime rate of interest quoted by Bloomberg on such date or on the most recent date when available from Bloomberg, or if not generally available from Bloomberg quoted by a similar reputable data source on such date or on the most recent date quoted, plus three percent (3.00%), calculated daily on the basis of a three hundred sixty-five (365) day year or, if lower, the highest rate permitted under applicable law, with such Default Interest accruing from, and including, the relevant payment date to, but excluding, the date on

[1] Include if a global note.
[2] Include if a global note.
[3] Include if a physical note.
[4] Include if a global note.
[5] Include if a physical note.

which such Defaulted Amounts shall have been paid by the Company. Upon the occurrence and during the continuance of any Specified Event of Default, Default Interest shall accrue and become payable at a per annum rate equal to four percent (4.00%) calculated daily on the basis of a three hundred sixty-five (365) day year or, if lower, the highest rate permitted under applicable law, upon the next occurring date on which Interest Payment is due, in each case in accordance with, and subject to the conditions and limitations set forth in, Section 2.03 and Section 6.02 of the Indenture.

Beginning with the Payment Measuring Period ending on June 30, 2020, and for each following Payment Measuring Period until the Payment Measuring Period ending on the End Date, within 75 days of the end of the applicable Payment Measuring Period, subject to the Aggregate Maximum Return Amount Qualification, the Company shall (i) provide notice to the Holders' Representative of any Payments due and payable in respect of the Notes and (ii) pay such Payments to each Depositary or its respective nominee, as the case may be, as the registered Holders of the Notes, in immediately available funds in lawful money of the United States; provided that (A) no Payments, Designated Default Interest or respective portions thereof shall be payable by the Company in respect of any period after the End Date, (B) no Payment, Designated Default Interest or respective portion thereof shall be payable by the Company to the extent that the Company has paid, or through payment of such Payments or Designated Default Interest will have paid, in excess of an aggregate sum of Payments and Designated Default Interest on account of the Notes equal to the Aggregate Maximum Return Amount (this clause (B) being referred to as the "**Aggregate Maximum Return Amount Qualification**") and (C) each Interest Payment in respect of the Notes shall be based solely on Net Revenues earned on U.S. sales of the Products in the applicable Payment Measuring Period, if any (the "**Limited Recourse Net Revenues**"), and in no event shall the Company be obligated to make any Interest Payment in respect of the Notes on account of any assets or properties other than the Limited Recourse Net Revenues (this clause (C) being referred to as the "**Limited Recourse Qualification**").

For the avoidance of doubt, (a) once Payments and Designated Default Interest in an aggregate amount equal to the Maximum Return Amount has been paid in respect of this Note (whether pursuant to this Note, pursuant to Article 14 of the Indenture, or otherwise), no further Payments or Designated Default Interest shall be payable on this Note, and no further Default Interest shall accrue with respect to any Specified Event of Default, (b) if and to the extent that Limited Recourse Net Revenues have not been generated, no amounts other than Principal Payments shall be payable on this Note, (c) if any portion of the Principal Amount in respect of any Note has not been paid as of the End Date, the Company shall pay such unpaid portion of the Principal Amount to the holder thereof notwithstanding the Limited Recourse Qualification and (d) in no event will Pfizer Inc. have any obligations to any Holder pursuant to the Indenture or this Note.

As provided in and subject to the provisions of the Indenture, the Company shall pay the Payments in respect of any Notes (other than Notes that are Global Notes) at the office or agency designated by the Company for that purpose. The Company has initially designated the Trustee as its Paying Agent and Note Registrar in respect of the Notes and its office in the United States

of America as a place where Notes may be presented for payment or for registration of transfer and exchange.

For purposes of this Note, the following terms shall have the meanings ascribed thereto:

"**Aggregate Principal Amount**" means the Principal Amounts in respect of all Notes then outstanding collectively, up to the aggregate amount of $120,000.

"**cUTI Indication**" means the complicated urinary tract infection indication;

"**cUTI Indication Payment Rate**" means 0.00025%; provided, that if the aggregate Principal Amounts in respect of all Notes issued and outstanding immediately after completion of the Rights Offering exceeds $80,000, the cUTI Indication Payment Rate means 0.00025% multiplied by a fraction, the numerator of which is $80,000, and the denominator of which is the aggregate Principal Amounts in respect of all Notes issued and outstanding immediately after completion of the Rights Offering.

"**Defaulted Amounts**" means any amounts on any Note that are due and payable but have not been paid or duly provided for.

"**Default Interest**" means interest accruing on Defaulted Amounts or upon the occurrence and during the continuance of Specified Events of Default.

"**Designated Default Interest**" means Default Interest that becomes due pursuant to Section 2.03(d)(ii) of the Indenture with respect to an Uncurable Event of Default.

"**End Date**" means December 31, 2045, or, in the event that no FDA Approvals have been obtained prior to December 31, 2025, such date.

"**Events of Default**" means the events of default set forth under Section 6.01 of the Indenture.

"**FDA**" means the United States Food and Drug Administration or any successor federal agency thereto.

"**FDA Approval**" means receipt by the Parent Guarantor (or a Subsidiary thereof) of approval of a new drug application and/or supplemental new drug application (or any successor form(s) or application(s) having substantially the same effect with respect to the approval of a drug for marketing and sale) by the FDA with respect to one or more Products for the uUTI Indication and/or cUTI Indication (as applicable).

"**GAAP**" means U.S. generally accepted accounting principles as in effect from time to time.

"**Gross Revenue**" means, as to any Products, for any Payment Measuring Period, the gross amount invoiced to and recognized as revenue on account of U.S. sales of such Products in

accordance with GAAP by the Parent Guarantor or its Subsidiaries with respect to the sale by the Parent Guarantor or its Subsidiaries or licensees or sublicensees of Products. For purposes of clarity, Gross Revenue shall not include amounts invoiced to and recognized as revenue on account of sales outside the U.S.

Notwithstanding the foregoing, in the event that a Product is sold in the U.S. together with one or more other therapeutically active ingredients or therapies not constituting the Product for a single price (regardless of their packaging) (a "**Combination Sale**"), the gross amount recognized as revenue by the Parent Guarantor or its Subsidiaries on account of such Combination Sale shall be determined as follows:

(i) Except as provided below, the gross amount recognized as revenue for a Combination Sale in the U.S. shall be calculated by multiplying the gross amount invoiced for the Combination Sale ("**Gross Combination Sale Amount**") by the fraction A/(A+B), where A is the wholesale acquisition cost charged by the Parent Guarantor or its Subsidiaries or any of their respective licensees (collectively, "**Sellers**") if such Product is sold separately in the U.S. by any of the Sellers, and B is the wholesale acquisition cost charged by the Sellers for the other product(s) or active ingredients/components included in the Combination Sale if such other product(s) or active ingredients/components are sold separately by the Sellers in the U.S.

(ii) In the event that the Sellers sell the Product included in a Combination Sale as a separate product in the U.S., but do not separately sell all of the other product(s) or active ingredients/components, as the case may be, included in such Combination Sale in the U.S., the calculation of the gross amount recognized as revenue resulting from such Combination Sale shall be determined by multiplying the Gross Combination Sale Amount by the fraction A/C where A is the wholesale acquisition cost charged by the Sellers for such Product sold separately in the U.S., and C is the wholesale acquisition cost charged by the Sellers in the U.S. for such Combination Product.

(iii) In the event that the Sellers do not sell the Product included in a Combination Sale as a separate product in the U.S., but do separately sell all of the other products or active ingredients/components, as the case may be, included in the Combination Sale the U.S., the calculation of the gross amount recognized as revenue resulting from such Combination Sale shall be determined by multiplying the Gross Combination Sale Amount by the fraction (C-D)/C, where C is the wholesale acquisition cost charged by the Sellers for such Combination Product sold separately in the U.S., and D is the aggregate of the wholesale acquisition cost charged by the Sellers in the U.S., as applicable, of such other product(s) or active ingredients/components, as the case may be, included in the Combination Product and sold separately in the U.S.

If the calculation of the gross amount recognized as revenue on account of such Combination Sale resulting from a Combination Sale in the U.S. cannot be determined by any of the foregoing methods, the calculation of the revenue from such Combination Sale shall be calculated in a manner determined by the Parent Guarantor in good faith based upon the relative

objective value of the active components of such Combination Product, in a manner consistent with GAAP.

"**Interest Payment**" means, as to any Note, for each Payment Measuring Period, the Payment on such Note, but only to the extent that such Payment is described in clause (1) of the definition of Payment hereunder.

"**IV Product**" means the sulopenem antibiotic being developed by the Parent Guarantor for intravenous delivery.

"**Maximum Return Amount**" means, as to any Note, the Maximum Return Amount set forth in such Note (which shall be 4,000 times the Principal Amount of such Note).

"**Maximum Return Amount Qualification**" means, as to any Note, the Maximum Return Amount Qualification set forth in such Note.

"**Minimum Principal Amount**" means $0.04.

"**Net Revenues**" means, as to any Products, for any Payment Measuring Period, the Gross Revenue in respect of such Products for such Payment Measuring Period, less the sum of the following to the extent attributable to activities in the U.S. that are incorporated in accordance with GAAP (except to the extent already excluded for Combination Sales in the definition of "Gross Revenue"): (a) customary sales returns actually made and allowances actually paid or taken, including trade, quantity and cash discounts, price adjustments, rebates, chargebacks, reimbursements or similar payments ordinarily granted or given but excluding discounts taken as part of bundling or other forms of multi-product purchase arrangements, (b) adjustments arising from consumer discount programs , (c) customs or excise duties, valued-added taxes, sales taxes, consumption taxes and other taxes (except income taxes) or duties relating to sales which are actually paid with respect to sales of Product, and (d) separately itemized freight and insurance incurred in shipping Product (to the extent that such costs are included in the amount invoiced to customers and included in Gross Revenue).

"**Oral Product**" means sulopenem etzadroxil and probenecid combined in a single bilayer tablet being developed by the Parent Guarantor for oral administration.

"**Payment**" means, as to any Note, for each Payment Measuring Period, any positive amount equal to the Pro Rata Share of such Note multiplied by the product of (a) the Net Revenues for such Payment Measuring Period, and (b) the applicable Payment Rate for such applicable Payment Measuring Period, subject to the End Date and the Maximum Return Amount Qualification; provided that each Payment on such Note shall be (1) an Interest Payment on such Note, to the extent that the amount of such Payment, when added to the amounts of all prior Payments on such Note, sums to an amount that is less than or equal to the difference of (x) the Maximum Return Amount for such Note less (y) the Principal Amount of such Note (such difference being the "Maximum Interest Payment Amount"), and (2) a Principal Payment on such Note, to the extent that the amount of such Payment, when added to the amounts of all prior

Payments on such Note, sums to an amount greater than the Maximum Interest Payment Amount.

"**Payment Measuring Period**" means a period equal to the prior six (6) months, calculated as of June 30 and December 31 of each calendar year during the term of this Indenture; provided no Payment Measuring Period shall commence after the End Date.

"**Payment Rate**" means, for each Payment Measuring Period, as measured at the end of such Payment Measuring Period: (a) for any Payment Measuring Period in which the Parent Guarantor (or Affiliate thereof) receives, or has previously received, FDA Approval for the uUTI Indication, a percentage equal to the uUTI Payment Rate multiplied by a number equal to the Aggregate Principal Amount; or (b) for any Payment Measuring Period in which the Parent Guarantor (or Affiliate thereof) receives, or has previously received, FDA Approval for the cUTI Indication, but has not received FDA Approval for the uUTI Indication, a percentage equal to the cUTI Indication Payment Rate multiplied by a number equal to the Aggregate Principal Amount.

"**Permitted Denomination**" means having a Principal Amount in any increment of the Minimum Principal Amount.

"**Principal Amount**" means, for any Note, the Principal Amount set forth in such Note (which shall be a Permitted Denomination).

"**Principal Payment**" means, as to any Note, for each Payment Measuring Period, the Payment on such Note, but only to the extent that such Payment is described in clause (2) of the definition of Payment hereunder.

"**Pro Rata Share**" means, as to any Note, a fraction, the numerator of which is the Principal Amount for such Note, and the denominator of which is the Aggregate Principal Amount.

"**Products**" means the Oral Product and the IV Product and "Product" means any one of them.

"**Rights Offering**" means any public offering of subscription rights to purchase units consisting of Notes and Exchangeable Senior Subordinated Notes by the Parent Guarantor and the Company to holders, at the date of this Indenture, of ordinary shares of the Parent Guarantor, nominal value $0.01 per share on a pro rata basis in accordance with their share ownership as of a record date to be determined by the Board of Directors of the Parent Guarantor or a committee thereof. The Initial Purchasers and their Affiliates shall not be entitled to purchase any units pursuant to the Rights Offering (regardless of whether or not under Irish or other applicable law such subscription rights are required to be offered to the Initial Purchasers).

"**Specified Events of Default**" means the Events of Default upon the occurrence and during the continuance of which Default Interest accrues pursuant to Section 2.03(d)(ii) of the Indenture.

"**Uncurable Event of Default**" means an Event of Default that has occurred pursuant to paragraphs (c) or (f) of Section 6.01 of the Indenture and is not by its nature subject to termination or cure.

"**uUTI Indication**" means the uncomplicated urinary tract infection indication.

"**uUTI Payment Rate**" means 0.00015%; provided, that if the aggregate Principal Amounts in respect of all Notes issued and outstanding immediately after completion of the Rights Offering exceeds $100,000, the uUTI Indication Payment Rate means 0.00015% multiplied by a fraction, the numerator of which is $100,000, and the denominator of which is the aggregate Principal Amounts in respect of all Notes issued and outstanding immediately after completion of the Rights Offering.

Reference is made to the further provisions of this Note set forth on the reverse hereof. Such further provisions shall for all purposes have the same effect as though fully set forth at this place.

This Note, and any claim, controversy or dispute arising under or related to this Note, shall be construed in accordance with and governed by the laws of the State of New York (without regard to the conflicts of laws provisions thereof).

In the case of any conflict between this Note and the Indenture, the provisions of the Indenture shall control and govern.

This Note shall not be valid or become obligatory for any purpose until the certificate of authentication hereon shall have been signed manually or by facsimile by the Trustee or a duly authorized authenticating agent under the Indenture.

[*Remainder of page intentionally left blank*]

IN WITNESS WHEREOF, the Company has caused this Note to be duly executed.

Iterum Therapeutics Bermuda Limited

By: _____
Name:
Title:

Dated:

TRUSTEE'S CERTIFICATE OF AUTHENTICATION

Computershare Trust Company, N.A.
as Trustee, certifies that this is one of the Notes described in the within-named Indenture.

By:_____
Authorized Signatory

[FORM OF REVERSE OF NOTE]

Iterum Therapeutics Bermuda Limited
Limited Recourse Royalty-Linked Subordinated Note

This Note is one of a duly authorized issue of Notes of the Company, designated as its Limited Recourse Royalty-Linked Subordinated Notes (the "**Notes**"), initially limited to Principal Amounts in the aggregate of $120,000, all issued or to be issued under and pursuant to an Indenture dated as of January 21, 2020 (the "**Indenture**"), between the Company, the Guarantors, the Holders' Representative and Computershare Trust Company, N.A. (the "**Trustee**"), to which Indenture and all indentures supplemental thereto reference is hereby made for a description of the rights, limitations of rights, obligations, duties and immunities thereunder of the Trustee, the Company, the Holders' Representative, the Guarantors and the Holders of the Notes. Capitalized terms used in this Note and not defined in this Note shall have the respective meanings set forth in the Indenture.

In case any Defaulted Amount, as defined in the Indenture, shall be payable and unpaid, Default Interest shall accrue thereon in accordance with the terms of the Indenture. Upon the occurrence and during the continuance of certain Events of Default, Default Interest shall accrue and become payable upon the next occurring date on which Interest Payment is due, in accordance with the terms of the Indenture.

The Indenture contains provisions permitting the Company, the Guarantors and the Trustee in certain circumstances, without the consent of the Holders of the Notes, and in certain other circumstances, with the consent of the Holders of Notes representing the right to receive no less than a majority of the aggregate Principal Amounts for all Notes then outstanding, on the terms and conditions set forth herein, evidenced as in the Indenture provided, to execute supplemental indentures modifying the terms of the Indenture and the Notes as described therein. It is also provided in the Indenture that, subject to certain exceptions, the Holders of Notes representing the right to receive a majority of the aggregate Principal Amounts for all Notes then outstanding, on the terms and conditions set forth herein, may on behalf of the Holders of all of the Notes waive any past Event of Default under Section 6.01 of the Indenture and its consequences.

Each Holder shall have the right to receive payment or delivery, as the case may be, of Principal Payments and Interest Payments for, and any accrued and unpaid Default Interest on, this Note at the place, at the respective times, at the rate and in the lawful money herein prescribed, subject in all events to the End Date, the Maximum Return Amount Qualification and the Limited Recourse Qualification.

For the avoidance of doubt, in no event will Pfizer Inc. have any obligations to any Holder pursuant to the Indenture or this Note.

The Notes are issuable in registered form without coupons in minimum denominations of the Principal Amount and multiples of the Principal Amount in excess thereof. At the office or

agency of the Company referred to on the face hereof, and in the manner and subject to the limitations provided in the Indenture, Notes may be exchanged for Notes of a like Permitted Denomination in the aggregate, without payment of any service charge but, if required by the Company or Trustee, with payment of a sum sufficient to cover any transfer or similar tax that may be imposed in connection therewith as a result of the name of the Holder of the new Notes issued upon such exchange of Notes being different from the name of the Holder of the old Notes surrendered for such exchange.

The Notes will be subject to optional redemption by the Company as set forth in Article 14 of the Indenture.

SCHEDULE A[6]

SCHEDULE OF EXCHANGES OF NOTES

Iterum Therapeutics Bermuda Limited
Limited Recourse Royalty-Linked Subordinated Note

The initial maximum Principal Amount of this Global Note is ONE HUNDRED TWENTY THOUSAND DOLLARS ($120,000). The following increases or decreases in the Principal Amount of this Global Note have been made:

Date of exchange	Amount of decrease in Principal Amount of this Global Note	Amount of increase in Principal Amount of this Global Note	Principal Amount of this Global Note following such decrease or increase	Signature of authorized signatory of Trustee or Custodian

[6] Include if a global note.

ATTACHMENT 1

[FORM OF ASSIGNMENT AND TRANSFER]

To: Computershare Trust Company, N.A., as Note Registrar

For value received _____ hereby sell(s), assign(s) and transfer(s) unto _____ (Please insert social security or Taxpayer Identification Number of assignee) the within Note, and hereby irrevocably constitutes and appoints _____ attorney to transfer the said Note on the books of the Company, with full power of substitution in the premises.

In connection with any transfer of the within Note occurring prior to the Resale Restriction Termination Date, as defined in the Indenture governing such Note, the undersigned confirms that such Note is being transferred, subject to the terms of the indenture:

□ To Iterum Therapeutics plc or a subsidiary thereof (including Iterum Therapeutics Bermuda Limited); or

□ Pursuant to a registration statement that has become or been declared effective under the Securities Act of 1933, as amended; or

□ Pursuant to and in compliance with Rule 144A under the Securities Act of 1933, as amended; or

□ Pursuant to and in compliance with Rule 144 under the Securities Act of 1933, as amended, or any other available exemption from the registration requirements of the Securities Act of 1933, as amended.

Dated: _____

_____

_____
Signature(s)

_____
Signature Guarantee

Signature(s) must be guaranteed by an eligible Guarantor Institution (banks, stock brokers, savings and loan associations and credit unions) with membership in an approved signature guarantee medallion program pursuant to Securities and Exchange Commission

Rule 17Ad-15 if Notes are to be delivered, other
than to and in the name of the registered holder.

NOTICE: The signature on the assignment must correspond with the name as written upon the face of the Note in every particular without alteration or enlargement or any change whatever.

Exhibit 4.6

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

As of December 31, 2019, Iterum Therapeutics plc ("we", "us" or the "Company") had one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"): our Ordinary Shares, $0.01 par value per share.

DESCRIPTION OF SHARE CAPITAL

The following description of our share capital is intended as a summary only and therefore is not a complete description of our share capital. This description is based upon, and is qualified by reference to, our Memorandum and Articles of Association (our "Constitution"), and applicable provisions of the Irish Companies Act 2014 (the "Irish Companies Act"). You should read our Constitution including our Articles of Association, which are filed as an exhibit to the Annual Report on Form 10-K of which this exhibit is a part, for the provisions that are important to you.

Capital Structure—Authorized Share Capital

Our authorized share capital consists of 50,000,000 ordinary shares of $0.01 each and 100,000,000 undesignated preferred shares of $0.01 each.

We may issue shares subject to the maximum authorized share capital contained in our Constitution. The authorized share capital may be increased or reduced (but not below the number of issued ordinary shares or preferred shares, as applicable) by a resolution approved by a simple majority of the votes of our shareholders cast at a general meeting (referred to under Irish law as an "ordinary resolution") (unless otherwise determined by the directors). The shares comprising our authorized share capital may be divided into shares of any nominal value.

The rights and restrictions to which the ordinary shares are subject are prescribed in our Articles of Association. Our Articles of Association entitle our board of directors, without shareholder approval, to determine the terms of our preferred shares. Preferred shares may be preferred as to dividends, rights upon liquidation or voting in such manner as our board of directors may resolve. The preferred shares may also be redeemable at the option of the holder of the preferred shares or at our option and may be convertible into or exchangeable for shares of any of our other class or classes, depending on the terms of such preferred shares.

Irish law does not recognize fractional shares held of record. Accordingly, our Articles of Association do not provide for the issuance of fractional shares, and our official Irish register will not reflect any fractional shares.

Whenever an alteration or reorganization of our share capital would result in any of our shareholders becoming entitled to fractions of a share, our board of directors may, on behalf of those shareholders that would become entitled to fractions of a share, arrange for the sale of the shares representing fractions and the distribution of the net proceeds of sale in due proportion among the shareholders who would have been entitled to the fractions.

Issuance of Shares

As a matter of Irish law, the board of directors of a company may issue authorized but unissued new shares without shareholder approval once authorized to do so by the Articles of Association of the company or by an ordinary resolution adopted by the shareholders at a general meeting. The authority conferred can be granted for a maximum period of five years, at which point it must be renewed by the shareholders by an ordinary resolution. Because of this requirement of Irish law, our Articles of Association authorize our board of directors to issue new shares up to the amount of our authorized but unissued share capital without shareholder approval for a period of five years from the date our Articles of Association were adopted.

Pre-emption Rights, Share Warrants and Share Options

Under Irish law certain statutory pre-emption rights apply automatically in favor of shareholders where shares are to be issued for cash. However, we have opted out of these pre-emption rights in our Articles of Association as permitted under Irish company law. Irish law requires this opt-out to be renewed every five years by a resolution approved by not less than 75% of the votes of our shareholders cast at a general meeting (referred to under Irish law as a "special resolution"). If the opt-out is not renewed, shares issued for cash must be offered to our existing shareholders on a *pro rata* basis to their existing shareholding before the shares can be issued to any newshareholders. The statutory pre-emption rights do not apply where shares are issued for non-cash consideration (such as in a share-for-share acquisition) and do not apply to the issue of non-equity shares (that is, shares that have the right to participate only up to a specified amount in any income or capital distribution) or where shares are issued pursuant to an employee share option or similar equity plan.

Pursuant to the terms of an Investor Rights Agreement (the "Investor Rights Agreement") entered into in connection with a private placement of our securities in January 2020, for so long as Sarissa Capital Management LP ("Sarissa") owns 10% of our outstanding ordinary shares on a fully diluted basis, Sarissa has a right of first offer with respect to our future proposed equity financings up to that portion of such new securities which equals Sarissa's, together with its affiliates, then-percentage ownership of our outstanding ordinary shares on a fully diluted basis, subject to specified exceptions for certain exempt issuances and pursuant to specified procedures. In the event our board of directors determines in good faith that we must conduct an equity financing on an expedited basis without compliance with the right of first offer described above in order to avoid material harm to us or any of our affiliates, we may effect and consummate such equity financing and, as promptly as practicable following the consummation of such equity financing, Sarissa will have the opportunity to participate in such equity financing and be put in the same place (including in respect of the percentage ownership of our equity securities) Sarissa would have been had such equity financing been effected in accordance with the terms of the right of first offer. As set forth in the Investor Rights Agreement, in any 12 month period, we may conduct an equity financing without compliance with the pre-emptive rights described above (an "Excused Issuance"); provided that we may not issue new securities (other than specified exempted securities) exceeding (in the aggregate with all other Excused Issuances during such 12 month period) 5% of the issued and outstanding ordinary shares on a fully diluted basis, and we may not issue new securities (other than specified exempted securities) in exchange for consideration (whether in cash or other property) the value of which exceeds (in the aggregate with all other Excused Issuances during such 12 month period) $5.0 million. We may only consummate two Excused Issuances for so long as the Investor Rights Agreement is in effect.

Our Articles of Association provide that, subject to any shareholder approval requirement under any laws, regulations or the rules of any stock exchange to which we are subject, the board of directors is authorized, from time to time, in its discretion, to grant such persons, for such periods and upon such terms as the board of directors deems advisable, options to purchase such number of shares of any class or classes or of any series of any class as the board of directors may deem advisable, and to cause warrants or other appropriate instruments evidencing such options to be issued. The Irish Companies Act provides that directors may issue share warrants or options without shareholder approval once authorized to do so by the Articles of Association. We are subject to the rules of the Nasdaq Global Market that require shareholder approval of certain equity plans and share issuances. Our board of directors may authorize the issuance of shares upon exercise of warrants or options without shareholder approval or authorization (up to the relevant authorized share capital limit).

Under Irish law, we are prohibited from allotting shares without consideration. Accordingly, at least the nominal value of the shares issued underlying any restricted share award, restricted share unit, performance share award, bonus share or any other share based grant must be paid pursuant to the Irish Companies Act.

Dividends

Under Irish law, dividends and distributions may only be made from distributable reserves. Distributable reserves, broadly, means the accumulated realized profits of a company, so far as not previously utilized by distribution or capitalization, less accumulated realized losses of a company, so far as not previously written off in a reduction or reorganization of capital, and includes reserves created by way of capital reduction, on a standalone basis. In addition, no distribution or dividend may be made unless our net assets are equal to, or in excess of, the aggregate of our called up share capital plus undistributable reserves and the distribution does not reduce our net assets below such aggregate. Undistributable reserves include the undenominated capital, the amount by which our accumulated unrealized profits, so far as not previously utilized by any capitalization, exceed our accumulated unrealized losses, so far as not previously written off in a reduction or reorganization of capital and any other reserve that we are prohibited from distributing by applicable law.

The determination as to whether or not we have sufficient distributable reserves to fund a dividend must be made by reference to the "relevant financial statements" of the Company. The "relevant financial statements" are either the last set of unconsolidated annual audited financial statements or unaudited financial statements properly prepared in accordance with the Irish Companies Act, which give a "true and fair view" of the Company's unconsolidated financial position in accordance with accepted accounting practice in Ireland. The "relevant financial statements" must be filed in the Companies Registration Office (the official public registry for companies in Ireland) prior to the making of the distribution.

Consistent with Irish law, our Articles of Association authorize the directors to declare interim dividends without shareholder approval out of funds lawfully available for the purpose, to the extent they appear justified by profits and subject always to the requirement to have distributable reserves at least equal to the amount of the proposed dividend. The board of directors may also recommend a dividend to be approved and declared by our shareholders at a general meeting. The board of directors may direct that the payment be made by distribution of assets, shares or cash and no dividend declared or paid may exceed the amount recommended by the directors. Dividends may be paid in U.S. dollars or any other currency.

Our directors may deduct from any dividend payable to any shareholder any amounts payable by such shareholder to us in relation to our shares.

Our directors may also authorize the issuance of shares with preferred rights to participate in our declared dividends. The holders of preferred shares may, depending on their terms, rank senior to our ordinary shares in terms of dividend rights and/or be entitled to claim arrears of a declared dividend out of subsequently declared dividends in priority to ordinary shareholders.

Share Repurchases, Redemptions and Conversions

Overview

Our Articles of Association provide that, in general, any ordinary share which we have agreed to acquire shall be deemed to be a redeemable share. Accordingly, for Irish company law purposes, the repurchase of ordinary shares by us may technically be effected as a redemption of those shares as described below under "—Repurchases and Redemptions." If our Articles of Association did not contain such provisions, all repurchases by us would be subject to many of the same rules that apply to purchases of our shares by subsidiaries described below under "—Purchases by Subsidiaries" including the shareholder approval requirements described below. Except where otherwise noted, when we refer to repurchasing or buying back our ordinary shares, we are referring to the redemption of ordinary shares by us pursuant to the Articles of Association or the purchase of our ordinary shares by a subsidiary of the Company, in each case in accordance with our Articles of Association and Irish law as described below.

Repurchases and Redemptions

Under Irish law, a company may issue redeemable shares and redeem them out of distributable reserves (which are described above under "Dividends") or, if the company proposes to cancel the shares on redemption, the proceeds of a new issue of shares for that purpose. The redemption of redeemable shares may only be made by us where the nominal value of the issued share capital that is not redeemable is not less than 10% of the nominal value of the total issued share capital of the company. All redeemable shares must also be fully-paid and the terms of redemption of the shares must provide for payment on redemption. Redeemable shares may, upon redemption, be cancelled or held in treasury. Based on the provisions of our articles described above, shareholder approval will not be required to redeem our shares.

We may also be given an additional general authority by our shareholders to purchase our own shares on-market, which would take effect on the same terms and be subject to the same conditions as applicable to purchases by our subsidiaries as described below.

Our board of directors may also issue preferred shares or other classes or series of shares which may be redeemed at either our option or the option of the shareholder, depending on the terms of such preferred shares. Please see "—Capital Structure—Authorized Share Capital."

Repurchased and redeemed shares may be cancelled or held as treasury shares. The nominal value of treasury shares held by us at any time must not exceed 10% of the nominal value of our issued share capital. We may not exercise any voting rights in respect of any shares held as treasury shares. Treasury shares may be cancelled by us or re-issued subject to certain conditions.

Purchases by Subsidiaries

Under Irish law, an Irish or non-Irish subsidiary of the Company may purchase our shares either as overseas market purchases on a recognized stock exchange such as the Nasdaq or off-market. For a subsidiary of ours to make market purchases of our shares, our shareholders must provide general authorization for such purchase by way of ordinary resolution. However, as long as this general authority has been granted, no specific shareholder authority for a particular market purchase by a subsidiary of our shares is required. We may elect to seek such general authority, which must expire no later than 18 months after the date on which it was granted, at our annual general meetings.

For an off-market purchase by a subsidiary of ours, the proposed purchase contract must be authorized by special resolution of the shareholders before the contract is entered into. The person whose shares are to be bought back cannot vote in favor of the special resolution and from the date of the notice of the meeting at which the resolution approving the contract is proposed, the purchase contract must be on display or must be available for inspection by shareholders at our registered office from the date of the notice of the meeting at which the resolution approving the contract is to be proposed.

In order for a subsidiary of ours to make an on-market purchase of our shares, such shares must be purchased on a "recognized stock exchange." The Nasdaq Global Market, on which our ordinary shares are listed, is specified as a recognized stock exchange for this purpose by Irish company law.

The number of shares held by our subsidiaries at any time will count as treasury shares and will be included in any calculation of the permitted treasury share threshold of 10% of the nominal value of our issued share capital. While a subsidiary holds shares of ours, it cannot exercise any voting rights in respect of those shares. The acquisition of our shares by a subsidiary of ours must be funded out of distributable reserves of the subsidiary.

Lien on Shares, Calls on Shares and Forfeiture of Shares

Our Articles of Association provide that we will have a first and paramount lien on every share for all debts and liabilities of any shareholder to the Company, whether presently due or not, payable in respect of such share. Subject to the terms of their allotment, directors may call for any unpaid amounts in respect of any shares to be paid, and if payment is not made within 14 days after notice demanding payment, we may sell the shares. These provisions are standard inclusions in the Articles of Association of an Irish company limited by shares and will only be applicable to our shares that have not been fully paid up. See "—Transfer and Registration of Shares."

Consolidation and Division; Subdivision

Under our Articles of Association, we may, by ordinary resolution (unless the directors determine otherwise), divide all or any of our issued share capital into shares of smaller nominal value than our existing shares (often referred to as a share split) or consolidate all or any of our issued share capital into shares of larger nominal value than is fixed by our memorandum of association (often referred to as a reverse share split), provided that the proportion between the amount paid for such share and the amount, if any, unpaid on each reduced share after the subdivision remains the same.

Reduction of Share Capital

We may, by ordinary resolution (unless the directors determine otherwise), reduce our authorized but unissued share capital in any way. We also may, by special resolution and subject to confirmation by the Irish High Court, reduce or cancel our issued share capital in any manner permitted by the Irish Companies Act.

Annual General Meetings of Shareholders

We are required to hold an annual general meeting within 18 months of incorporation and at intervals of no more than 15 months thereafter, provided that an annual general meeting is held in each calendar year following the first annual general meeting and no more than nine months after our fiscal year-end. Any annual general meeting may be held outside Ireland, provided that technological means are provided to enable shareholders to participate in the meeting without leaving Ireland.

Notice of an annual general meeting must be given to all of our shareholders and to our auditors. Our Articles of Association provide for a minimum notice period of 21 clear days (i.e. 21 days excluding the day when the notice is given or deemed to be given and the day of the event for which it is given or on which it is to take effect), which is the minimum permitted under Irish law.

The only matters which must, as a matter of Irish company law, be transacted at an annual general meeting are (i) the consideration of the statutory financial statements, report of the directors, report of the statutory auditors, (ii) review by the members of the company's affairs and (iii) the appointment or re-appointment of the statutory auditors.

At any annual general meeting, only such business may be conducted as has been brought before the meeting:

- in the notice of the meeting;
- by or at the direction of the board of directors;
- in certain circumstances, at the direction of the Irish High Court;
- as required by law; or
- that the chairman of the meeting determines is properly within the scope of the meeting.

In addition, and subject to compliance with our Articles of Association, shareholders entitled to vote at an annual general meeting may propose business in advance of the meeting to be considered thereat.

Extraordinary General Meetings of Shareholders

Our extraordinary general meetings may be convened by (i) the board of directors, (ii) on requisition of the shareholders holding not less than 10% of our paid up share capital carrying voting rights, (iii) in certain circumstances, on requisition of our auditors; or (iv) in exceptional cases, by order of the Irish High Court.

Extraordinary general meetings are generally held for the purpose of approving shareholder resolutions as may be required from time to time. At any extraordinary general meeting, only such business will be conducted as is set forth in the notice thereof or is proposed pursuant to and in accordance with the procedures and requirements set out in our Articles of Association.

Notice of an extraordinary general meeting must be given to all of our shareholders and to our auditors. Under Irish law and our Articles of Association, the minimum notice periods are 21 clear days' notice in writing for an extraordinary general meeting to approve a special resolution and 14 clear days' notice in writing for any other extraordinary general meeting.

In the case of an extraordinary general meeting convened by our shareholders, the proposed purpose of the meeting must be set out in the requisition notice. Upon receipt of any such valid requisition notice, our board of directors has 21 days to convene a meeting of our shareholders to vote on the matters set out in the requisition notice. This meeting must be held within two months of the receipt of the requisition notice. If the board of directors does not convene the meeting within such 21day period, the requisitioning shareholders, or any of them representing more than one half of the total voting rights of all of them, may themselves convene a meeting, which meeting must be held within three months of our receipt of the requisition notice.

If the board of directors becomes aware that our net assets are not greater than half of the amount of our called-up share capital, our directors must convene an extraordinary general meeting of our shareholders not later than 28 days from the date that the fact is known to a director to be held not later than 56 days from such date. This meeting must be convened for the purposes of considering whether any, and if so what, measures should be taken to address the situation.

Quorum for General Meetings

Our Articles of Association provide that no business shall be transacted at any general meeting unless a quorum is present. One or more shareholders present in person or by proxy at any meeting of shareholders holding not less than a majority of the issued shares that carry the right to vote at the meeting constitutes a quorum for the conduct of any business at a general meeting.

Voting

Our Articles of Association provide that all votes at a general meeting will be decided on a poll and that the board or the chairman may determine the manner in which the poll is to be taken and the manner in which the votes are to be counted.

Every shareholder is entitled to one vote for each ordinary share that he or she holds as of the record date for the meeting. Voting rights may be exercised by shareholders registered in our share register as of the record date for the meeting or by a duly appointed proxy, which proxy need not be a shareholder. Where interests in shares are held by a nominee trust company, this company may exercise the rights of the beneficial holders on their behalf as their proxy. All proxies must be appointed in the manner prescribed by our Articles of Association, which provide that our board of directors may permit shareholders to notify us of their proxy appointments electronically.

In accordance with our Articles of Association, our directors may from time to time authorize the issuance of preferred shares or any other class or series of shares. These shares may have such voting rights as may be specified in the terms of such shares (e.g., they may carry more votes per share than ordinary shares or may entitle their holders to a class vote on such matters as may be satisfied in the terms of such shares). Treasury shares or shares of ours that are held by our subsidiaries will not be entitled to be voted at general meetings of shareholders.

Irish company law requires special resolutions of the shareholders at a general meeting to approve certain matters. Examples of matters requiring special resolutions include:

- amending the objects as contained in our memorandum of association;
- amending our Articles of Association;
- approving a change of name;
- authorizing the entering into of a guarantee or provision of security in connection with a loan, quasi-loan or credit; transaction to a director or connected person;
- opting out of pre-emption rights on the issuance of new shares;
- re-registration from a public limited company to a private company;
- purchase of own shares off-market;
- reduction of issued share capital;
- sanctioning a compromise/scheme of arrangement;
- resolving that the company be wound up by the Irish courts;
- resolving in favor of a shareholders' voluntary winding-up;
- re-designation of shares into different share classes;
- setting the re-issue price of treasury shares; and
- variation of class rights attaching to classes of shares (where our Articles of Association do not provide otherwise).

Neither Irish law nor any of our constituent documents places limitations on the right of non-resident or foreign owners to vote or hold our shares.

Variation of Rights Attaching to a Class or Series of Shares

Under our Articles of Association and the Irish Companies Act, any variation of class rights attaching to our issued shares must be approved by an ordinary resolution passed at a general meeting of the shareholders of the affected class or with the consent in writing of the holders of a majority of the issued shares of that class of shares entitled to vote on such variation. The rights conferred upon the holder of any pre-existing issued shares shall not be deemed to be varied by the issuance of any preferred shares.

The provisions of our Articles of Association relating to general meetings apply to general meetings of the holders of any class of shares except that the necessary quorum is determined in reference to the shares of the holders of the class. Accordingly, for general meetings of holders of a particular class of shares, a quorum consists of one or more shareholders present in person or by proxy holding not less than a majority of the issued and outstanding shares of the class entitled to vote at the meeting in question.

Record Date

Our Articles of Association provide that the board may fix in advance a date as the record date (i) for any such determination of members entitled to notice of or to vote at a general meeting of the members, which record date shall not be more than 60 days before the date of such meeting, and (ii) for the purpose of determining the members entitled to receive payment of any dividend or other distribution, or in order to make a determination of members for any other proper purpose, which record date shall not be more than 60 days prior to the date of payment of such dividend or other distribution or the taking of any action to which such determination of members is relevant.

If no record date is fixed for the determination of members entitled to notice of or to vote at a meeting of members, the date immediately preceding the date on which notice of the meeting is deemed given under our Articles of Association will be the record date for such determination of members.

Shareholder Proposals

Under Irish law, there is no general right for a shareholder to put items on the agenda of an annual general meeting of a U.S.-listed company, other than as set out in the Articles of Association of a company. Under our Articles of Association, in addition to any other applicable requirements, for business or nominations to be properly brought before an annual general meeting by a shareholder, such shareholder must have given timely notice thereof in proper written form to our corporate secretary.

To be timely for an annual general meeting, a shareholder's notice to our secretary as to the business or nominations to be brought before the meeting must be delivered to or mailed and received at our registered office (i) with respect to our first annual general meeting as a public limited company, not later than the 10th day following the day on which public announcement of the date of such annual general meeting is made and (ii) with respect to all other annual general meetings not less than 90 days nor more than 120 days before the first anniversary of the notice convening our annual general meeting for the prior year. In the event that the date of the annual general meeting is changed by more than 30 days from the first anniversary date of the preceding year's annual general meeting, notice by the member must be so delivered by close of business on the day that is not earlier than 120 days prior to such annual general meeting and not later than the close of business on the later of (a) 90 days prior to the day of the contemplated annual general meeting or (b) ten days after the day on which public announcement of the date of the contemplated annual general meeting is first made by us. In no event shall the public announcement of an adjournment or postponement of an annual general meeting commence a new time period (or extend any time period) for the giving of a shareholder's notice.

To be timely for business or nominations of a director at an extraordinary general meeting, notice must be delivered, or mailed and received not less than 90 days nor more than 120 days prior to the date of such extraordinary general meeting or, if the first public announcement of the date of the extraordinary general meeting is less than 100 days prior to the date of the meeting, by close of business ten days after the day on which the public announcement of the date of the extraordinary general meeting is first made by us.

For nominations to the board, the notice must include all information about the director nominee that is required to be disclosed by U.S. Securities and Exchange Commission rules regarding the solicitation of proxies for the election of directors pursuant to Regulation 14A under the Exchange Act. For other business that a shareholder proposes to bring before the meeting, the notice must include a brief description of the business, the reasons for proposing the business at the meeting and a discussion of any material interest of the shareholder in the business. Whether the notice relates to a nomination to the board of directors or to other business to be proposed at the meeting, the notice also must include information about the shareholder and the shareholder's holdings of our shares. The chairman of the meeting shall have the power and duty to determine whether any business proposed to be brought before the meeting was made or proposed in accordance with these procedures (as set out in our Articles of Association), and if any proposed business is not in compliance with these provisions, to declare that such defective proposal shall be disregarded.

Shareholders' Suits

In Ireland, the decision to institute proceedings on behalf of a company is generally taken by the company's board of directors. In certain limited circumstances, a shareholder may be entitled to bring a derivative action on our behalf. The central question at issue in deciding whether a minority shareholder may be permitted to bring a derivative action is whether, unless the action is brought, a wrong committed against us would otherwise go unredressed. The cause of action may be against a director, another person or both.

A shareholder may also bring proceedings against us in his or her own name where the shareholder's rights as such have been infringed or where our affairs are being conducted, or the powers of the board of directors are being exercised, in a manner oppressive to any shareholder or shareholders or in disregard of their interests as shareholders. Oppression connotes conduct that is burdensome, harsh or wrong. This is an Irish statutory remedy under Section 212 of the Irish Companies Act and the court can grant any order it sees fit, including providing for the purchase or transfer of the shares of any shareholder.

Inspection of Books and Records

Under Irish law, shareholders have the right to: (i) receive a copy of our Constitution; (ii) inspect and obtain copies of the minutes of general meetings and any resolutions; (iii) inspect and receive a copy of the register of shareholders, register of directors and secretaries, register of directors' interests and other statutory registers maintained by us; (iv) inspect copies of directors' service contracts; (v) inspect copies of instruments creating charges; (vi) receive copies of statutory financial statements and directors' and auditors' reports which have previously been sent to shareholders prior to an annual general meeting; and (vii) receive financial statements of a subsidiary company of ours which have previously been sent to shareholders prior to an annual general meeting for the preceding ten years. Our auditors will also have the right to inspect all of our books, records and vouchers. The auditors' report must be circulated to the shareholders with our financial statements prepared in accordance with Irish law with the notice of annual general meeting and must be presented to our shareholders at our annual general meeting.

Acquisitions

There are a number of mechanisms for acquiring an Irish public limited, including:

- a court-approved scheme of arrangement under the Irish Companies Act. A scheme of arrangement with one or more classes of shareholders requires a court order from the Irish High Court and the approval of (i) more than 50% in number of the shareholders of each participating class or series voting on the scheme of arrangement, and (ii) representing 75% in value of the shares of such participating class or series held by the shareholders voting on the scheme of arrangement, in each case at the relevant meeting or meetings. A scheme of arrangement, if authorized by the shareholder of each participating class or series and the court, is binding on all of the shareholders of each participating class or series;

- through a tender or takeover offer by a third party, in accordance with the Irish Takeover Rules and the Irish Companies Act, for all of our shares. Where the holders of 80% or more of our shares (excluding any shares already beneficially owned by the bidder) have accepted an offer for their shares, the remaining shareholders may also be statutorily required to transfer their shares, unless, within one month, the non-tendering shareholders can obtain an Irish court order otherwise providing. If the offeror has acquired acceptances of 80% of all of our shares but does not exercise its "squeeze-out" right, then the non-accepting shareholders also have a statutory right to require the bidder to acquire their shares on the same terms as the original offer, or such other terms as the bidder and the non-tendering shareholders may agree or on such term as an Irish court, on application of the bidder or non-tendering shareholder, may order. If our shares were to be listed on the Euronext Dublin or another regulated stock exchange in the European Union, the aforementioned 80% threshold would be increased to 90%;

- by way of a transaction with a company incorporated in the European Economic Area which includes all member states of the European Union and Norway, Iceland and Liechtenstein ("EEA") under the European Communities (Cross-Border Mergers) Regulations 2008 (as amended). Such a transaction must be approved by a special resolution and by the Irish High Court. If we are being merged with another EEA company under the EU Cross-Border Mergers Directive (EU) 2019/2121 and the consideration payable to our shareholders is not all in the form of cash, our shareholders may be entitled to require their shares to be acquired at fair value; and

- by way of a merger with another Irish company under the Irish Companies Act which must be approved by a special resolution and by the Irish High Court.

Appraisal Rights

Generally, under Irish law, shareholders of an Irish company do not have statutory appraisal rights. If we are being merged as the transferor company with another EEA company under the European Communities (Cross-Border Merger) Regulations 2008 (as amended) or if we are being merged with another Irish company under the Irish Companies Act, (i) any of our shareholders who voted against the special resolution approving the merger or (ii) if 90% of our shares are held by the successor company, any other of our shareholders, may be entitled to require that the successor company acquire its shares for cash.

Disclosure of Interests in Shares

Under the Irish Companies Act, there is a notification requirement for shareholders who acquire or cease to be interested in 3% of the shares of an Irish public limited company. Our shareholders must therefore make such a notification to us if, as a result of a transaction, the shareholder will become interested in 3% or more of our shares or if, as a result of a transaction, a shareholder who was interested in 3% or more of our shares ceases to be so interested. Where a shareholder is interested in 3% or more of our shares, the shareholder must notify us of any alteration of his or her interest that brings his or her total holding through the nearest whole percentage number, whether an increase or a reduction. The relevant percentage figure is calculated by reference to the aggregate nominal value of the shares in which the shareholder is interested as a proportion of the entire nominal value of our issued share capital (or any such class of share capital in issue). Where the percentage level of the shareholder's interest does not amount to a whole percentage, this figure may be rounded down to the next whole number. All such disclosures should be notified to us within five business days of the transaction or alteration of the shareholder's interests that gave rise to the notification requirement. If a shareholder fails to comply with these notification requirements, the shareholder's rights in respect of any of our shares it holds will not be enforceable, either directly or indirectly. However, such person may apply to the court to have the rights attaching to such shares reinstated.

In addition to these disclosure requirements, under the Irish Companies Act, we may by notice in writing, require a person whom we know or have reasonable cause to believe to be, or at any time during the three years immediately preceding the date on which such notice is issued to have been, interested in shares comprised in our relevant share capital to: (i) indicate whether or not it is the case and (ii) where such person holds or has during that time held an interest in our ordinary shares, to provide additional information, including the person's own past or present interests in our shares. If the recipient of the notice fails to respond within the reasonable time period specified in the notice, we may apply to court for an order directing that the affected shares be subject to certain restrictions, as prescribed by the Irish Companies Act, as follows:

- any transfer of those shares, or in the case of unissued shares any transfer of the right to be issued with shares and any issue of shares, will be void;
- no voting rights will be exercisable in respect of those shares;
- no further shares will be issued in right of those shares or in pursuance of any offer made to the holder of those shares; and
- no payment will be made of any sums due from us on those shares, whether in respect of capital or otherwise.

Where our shares are subject to these restrictions, the court may order the shares to be sold and may also direct that the shares shall cease to be subject to these restrictions.

In the event we are in an offer period pursuant to the Irish Takeover Rules, accelerated disclosure provisions apply for persons holding an interest in our securities of 1.0% or more.

Irish Takeover Rules

A transaction in which a third party seeks to acquire 30% or more of our voting rights will be governed by the Irish Takeover Panel Act 1997 and the Irish Takeover Rules made thereunder and will be regulated by the Irish Takeover Panel. The "General Principles" of the Irish Takeover Rules and certain important aspects of the Irish Takeover Rules are described below.

General Principles

The Irish Takeover Rules are built on the following General Principles, which will apply to any transaction regulated by the Irish Takeover Panel:

- in the event of an offer, all holders of securities of the target company should be afforded equivalent treatment and, if a person acquires control of a company, the other holders of securities must be protected;
- the holders of the securities in the target company must have sufficient time and information to enable them to reach a properly informed decision on the offer;
- where it advises the holders of securities, the board of the target company must give its views on the effects of implementation of the offer on employment, conditions of employment and the locations of the target company's places of business;
- the board of the target company must act in the interests of the company as a whole and must not deny the holders of securities the opportunity to decide on the merits of the offer;
- false markets must not be created in the securities of the target company, the bidder or of any other company concerned by the offer in such a way that the rise or fall of the prices of the securities becomes artificial and the normal functioning of the markets is distorted;
- a bidder must announce an offer only after ensuring that he or she can fulfil in full, any cash consideration, if such is offered, and after taking all reasonable measures to secure the implementation of any other type of consideration;

- a target company must not be hindered in the conduct of its affairs for longer than is reasonable by an offer for its securities; and
- a substantial acquisition of securities (whether such acquisition is to be effected by one transaction or a series of transactions) shall take place only at an acceptable speed and shall be subject to adequate and timely disclosure.

Mandatory Bid

Under certain circumstances, a person who acquires shares or other of our voting rights may be required under the Irish Takeover Rules to make a mandatory cash offer for our remaining outstanding shares at a price not less than the highest price paid for the shares by the acquirer (or any parties acting in concert with the acquirer) during the previous 12 months. This mandatory bid requirement is triggered if an acquisition of shares would (i) increase the aggregate holding of an acquirer (including the holdings of any parties acting in concert with the acquirer) to shares representing 30% or more of our voting rights, or (ii) in the case of a person holding (together with its concert parties) shares representing 30% or more of our voting rights, after giving effect to the acquisition, increase the percentage of the voting rights held by that person (together with its concert parties) by 0.05% within a 12-month period. Any person (excluding any parties acting in concert with the holder) holding shares representing more than 50% of the voting rights of a company is not subject to these mandatory offer requirements in purchasing additional securities.

Voluntary Bid; Requirements to Make a Cash Offer and Minimum Price Requirements

A voluntary offer is an offer that is not a mandatory offer. If a person makes a voluntary offer to acquire outstanding ordinary shares of ours, the offer price must be no less than the highest price paid for our shares by the bidder or its concert parties during the three-month period prior to the commencement of the offer period. The Irish Takeover Panel has the power to extend the "look back" period to 12 months if the Irish Takeover Panel, taking into account the General Principles, believes it is appropriate to do so.

If the bidder or any party acting in concert with it has acquired our ordinary shares (i) during the period of 12 months prior to the commencement of the offer period which represent more than 10% of our total ordinary shares or (ii) at any time after the commencement of the offer period, the offer must be in cash (or accompanied by a full cash alternative) and the price per ordinary share must not be less than the highest price paid by the bidder or any party acting in concert with it during, in the case of (i), the 12-month period prior to the commencement of the offer period and, in the case of (ii), the offer period. The Irish Takeover Panel may apply this rule to a bidder who, together with any party acting in concert with it, has acquired less than 10% of our total ordinary shares in the 12-month period prior to the commencement of the offer period if the Irish Takeover Panel, taking into account the General Principles, considers it just and proper to do so.

An offer period will generally commence from the date of the first announcement of the offer or proposed offer.

Substantial Acquisition Rules

The Irish Takeover Rules also contain rules governing substantial acquisitions of shares which restrict the speed at which a person may increase his or her holding of shares and rights over shares to an aggregate of between 15% and 30% of our voting rights. Except in certain circumstances, an acquisition or series of acquisitions of shares or rights over shares representing 10% or more of our voting rights is prohibited if such acquisition(s), when aggregated with shares or rights already held, would result in the acquirer holding 15% or more but less than 30% of our voting rights and such acquisitions are made within a period of seven days. These rules also require accelerated disclosure of acquisitions of shares or rights over shares relating to such holdings.

Anti-Takeover Provisions

Shareholder Rights Plan

Our Articles of Association expressly authorize our board of directors to adopt a shareholder rights plan, subject to applicable law.

Frustrating Action

Under the Irish Takeover Rules, our board of directors is not permitted to take any action which might frustrate an offer for our shares once our board of directors has received an approach which may lead to an offer or has reason to believe an offer is imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of shares, options or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any time during which the board of directors has reason to believe an offer is imminent. Exceptions to this prohibition are available where:

- the action is approved by our shareholders at a general meeting; or
- the Irish Takeover Panel has given its consent, where:
    - it is satisfied the action would not constitute frustrating action;

- our shareholders that hold 50% of the voting rights state in writing that they approve the proposed action and would vote in favor of it at a general meeting;

- the action is taken in accordance with a contract entered into prior to the announcement of the offer; or

- the decision to take such action was made before the announcement of the offer and either has been at least partially implemented or is in the ordinary course of business.

Business Combinations with Interested Shareholders

Our Articles of Association provide that, subject to certain exceptions, we may not engage in certain business combinations with any person that acquires beneficial ownership of 15% or more of our outstanding voting shares for a period of three years following the date on which the person became a 15% shareholder unless: (i) prior to the date on which the person becomes a 15% shareholder, a committee of our disinterested directors approved the business combination; and (ii) in certain circumstances, the business combination is authorized by a special resolution of disinterested shareholders.

Further Provisions

Certain other provisions of Irish law or our Constitution may be considered to have anti-takeover effects, including advance notice requirements for director nominations and other shareholder proposals, as well as those described under the headings "—Capital Structure—Authorized Share Capital" (regarding issuance of preferred shares), "—Pre-emption Rights, Share Warrants and Share Options," "—Disclosure of Interests in Shares," "—Appointment of Directors," and "—Removal of Directors."

Insider Dealing

The Irish Takeover Rules also provide that no person, other than the bidder, who is privy to confidential price-sensitive information concerning an offer made in respect of the acquisition of a company (or a class of its securities) or a contemplated offer shall deal in relevant securities of the target during the period from the time at which such person first has reason to suppose that such an offer, or an approach with a view to such an offer being made, is contemplated to the time of (i) the announcement of such offer or approach or (ii) the termination of discussions relating to such offer, whichever is earlier.

Corporate Governance

Our Articles of Association allocate authority over the day-to-day management of the Company to the board of directors. Our board of directors may then delegate management of the Company to committees of the board or such other persons as it thinks fit. Regardless of any delegation, the board of directors will remain responsible, as a matter of Irish law, for the proper management of the affairs of our Company. The board of directors may create new committees or change the responsibilities of existing committees from time to time. Committees may meet and adjourn as they determine proper. Unless otherwise determined by the board of directors, the quorum necessary for the transaction of business at any committee meeting shall be a majority of the members of the committee.

Appointment of Directors

The Irish Companies Act provides for a minimum of two directors. Our Articles of Association provide that the number of directors will be not less than two and not more than 13. The authorized number of directors within the prescribed range will be determined solely by our board of directors and does not require approval or ratification by the shareholders in a general meeting. Our directors will be elected by way of an ordinary resolution at a general meeting save that directors in contested elections will be elected by a plurality of the votes of the shares present in person or represented by proxy at the relevant general meeting and entitled to vote on the election of directors. If the number of the directors is reduced below the fixed minimum number, the remaining director or directors may appoint an additional director or additional directors to make up such minimum or may convene a general meeting for the purpose of making such appointment. Casual vacancies may be filled by the board of directors.

Our Articles of Association provide that our board of directors is divided into three classes serving staggered three-year terms. Shareholders do not have cumulative voting rights. Accordingly, the holder of a majority of the voting rights attaching to our ordinary shares will, as a practical matter, be entitled to control the election of all directors. At each annual general meeting, directors will be elected for a full term of three years to succeed those directors of the relevant class whose terms are expiring.

Under our Articles of Association, our board of directors has the authority to appoint directors to the board either to fill a vacancy or as an additional director. A vacancy on the board of directors created by the removal of a director may be filled by an ordinary resolution of the shareholders at the meeting at which such director is removed and, in the absence of such election or appointment, the remaining directors may fill the vacancy. The board of directors may fill a vacancy by an affirmative vote of a majority of the directors constituting a quorum. If there is an insufficient number of directors to constitute a quorum, the board may nonetheless act to fill such vacancies or call a general meeting of the shareholders. Under our Articles of Association, if the board fills a vacancy, the director will hold this position as a director for a term that will coincide with the remaining term of the relevant class of director. If there is an appointment to fill a casual vacancy or an addition to the board, the total number of directors shall not at any time exceed the number of directors from time to time fixed by the board in accordance with our Articles of Association.

Pursuant to the terms of the Investor Rights Agreement, for so long as Sarissa and its affiliates own at least 5% or 12.5%, as applicable, of our outstanding ordinary shares on a fully diluted basis, promptly, and in any event no more than 5 business days following written request of Sarissa, we will cause our board of directors to increase to consist of nine or 10 members, as applicable, and we will cause our board of directors to consist of no more than 10 members without the prior written consent of Sarissa. In addition, for so long as Sarissa and its affiliates own at least 12.5% of our outstanding ordinary shares on a fully diluted basis, Sarissa will have the right to designate two directors to our board of directors and, for so long as Sarissa and its affiliates own at least 5% but less than 12.5%, it will have the right to designate one director to our board of directors (the "Investor Designees"). Pursuant to the terms of the Investor Rights Agreement, such Investor Designees will be appointed to our board of directors and to be members of the class of directors that was subject to reelection at our most recent annual general meeting of shareholders. The Investor Designees will be entitled to be a member of any committee of the board of directors subject to the terms of the Investor Rights Agreement. Pursuant to the terms of the Investor Rights Agreement, the Private Placement Investors, subject to specified exceptions, have agreed with us to vote in favor of the election of the Investor Designees, and we have agreed to cause the Investor Designees to be named in any relevant proxy statement.

Removal of Directors

The Irish Companies Act provides that, notwithstanding anything contained in the Articles of Association of a company or in any agreement between that company and a director, the shareholders may, by an ordinary resolution, remove a director from office before the expiration of his or her term, provided that notice of the intention to move any such resolution be given by the shareholders to the company not less than 28 days before the meeting at which the director is to be removed, and the director will be entitled to be heard at such meeting. The power of removal is without prejudice to any claim for damages for breach of contract (e.g., employment agreement) that the director may have against us in respect of his or her removal.

Director Interested Transactions

Under the Irish Companies Act and our Articles of Association, a director who has an interest in a proposal, arrangement or contract is required to declare the nature of his or her interest at the first opportunity either (i) at a meeting of the board at which such proposal, arrangement or contract is first considered (provided such director knows this interest then exists, or in any other case, at the first meeting of the board after learning that he or she is or has become so interested) or (ii) by providing a general notice to the directors declaring that he or she is to be regarded as interested in any proposal, arrangement or contract with a particular person, and after giving such general notice will not be required to give special notice relating to any particular transaction. Provided the interested director makes such required disclosure, he or she shall be counted in determining the presence of a quorum at a meeting regarding the relevant proposal, arrangement or contract and will be permitted to vote on such proposal, arrangement or contract.

Pursuant to our Articles of Association, it is within the directors' sole discretion to determine their compensation.

Borrowing

Pursuant to our Articles of Association, among the directors' powers are the right to borrow money and to mortgage or charge the Company's undertaking, property and uncalled capital or any part thereof and to issue debentures, debenture stock, mortgages, bonds or such other securities whether outright or as security for any debt, liability or obligation of the Company or of any third party.

Duration; Dissolution; Rights upon Liquidation

Our duration will be unlimited. We may be dissolved and wound up at any time by way of a shareholders' voluntary winding up or a creditors' winding up. In the case of a shareholders' voluntary winding-up, a special resolution of shareholders is required. We may also be dissolved by way of court order on the application of a creditor, or by the Companies Registration Office as an enforcement measure where we have failed to file certain returns. We may also be dissolved by the Director of Corporate Enforcement in Ireland where the affairs of the Company have been investigated by an inspector and it appears from the report or any information obtained by the Director of Corporate Enforcement that we should be wound up.

The rights of the shareholders to a return of our assets on dissolution or winding up, following the settlement of all claims of creditors, are prescribed in our Articles of Association or the terms of any shares issued by the directors from time to time. The holders of preferred shares in particular may have the right to priority in a dissolution or winding up. If the Articles of Association and terms of issue of the shares of the Company contain no specific provisions in respect of a dissolution or winding up then, subject to the shareholder priorities and the rights of any creditors, the assets will be distributed to shareholders in proportion to the paid-up nominal value of the shares held. Our Articles of Association provide that our ordinary shareholders may be entitled to participate in a winding up, and the method by which the property will be divided shall be determined by the liquidator, subject to a special resolution of the shareholders, but such rights of ordinary shareholders to participate may be subject to the rights of any preferred shareholders to participate under the terms of any series or class of preferred shares.

Share Certificates

Pursuant to the Irish Companies Act, a shareholder is entitled to be issued a share certificate on request and subject to payment of a nominal fee.

Stock Exchange Listing

Our ordinary shares are listed on the Nasdaq Global Market under the symbol "ITRM." Our ordinary shares are not listed on the Euronext Dublin.

No Sinking Fund

Our shares have no sinking fund provisions.

Transfer and Registration of Shares

Our transfer agent is Computershare Trust Company, N.A. The transfer agent maintains our share register, and registration in the share register will be determinative of membership in us. A shareholder of ours who only holds shares beneficially will not be the holder of record of such shares. Instead, the depository or other nominee will be the holder of record of those shares. Accordingly, a transfer of shares from a person who holds such shares beneficially to a person who also holds such shares beneficially through a depository or other nominee will not be registered in our official share register, as the depository or other nominee will remain the record holder of any such shares.

A written instrument of transfer is required under Irish law in order to register on our official share register any transfer of shares (i) from a person who holds such shares directly to any other person, (ii) from a person who holds such shares beneficially to a person who holds such shares directly or (iii) from a person who holds such shares beneficially to another person who holds such shares beneficially where the transfer involves a change in the depository or other nominee that is the record owner of the transferred shares. An instrument of transfer is also required for a shareholder who directly holds shares to transfer those shares into his or her own broker account (or vice versa). Such instruments of transfer may give rise to Irish stamp duty, which must be paid prior to registration of the transfer on our official Irish share register. However, a shareholder who directly holds shares may transfer those shares into his or her own broker account (or vice versa) without giving rise to Irish stamp duty provided there is no change in the ultimate beneficial ownership of the shares as a result of the transfer and the transfer is not made in contemplation of a sale of the shares.

Any transfer of our shares that is subject to Irish stamp duty will not be registered in the name of the buyer unless an instrument of transfer is duly stamped and provided to our transfer agent. Our Articles of Association allow us, in our absolute discretion, to create an instrument of transfer and pay (or procure the payment of) any stamp duty, which is the legal obligation of a transferee. In the event of any such payment, we are (on behalf of ourselves or our affiliates) entitled to (i) seek reimbursement from the transferee or transferor (at its discretion), (ii) set-off the amount of the stamp duty against future dividends payable to the transferee or transferor (at its discretion) and (iii) have a lien against the shares on which it has paid stamp duty. Parties to a share transfer may assume that any stamp duty arising in respect of a transaction in our shares has been paid unless one or both of such parties is otherwise notified by us.

Our Articles of Association delegate to our secretary (or such other person as may be nominated by the secretary for this purpose) the authority to execute an instrument of transfer on behalf of a transferring party.

Our Articles of Association grant our board of directors general discretion to decline to register an instrument of transfer unless the transfer is in respect of one class of shares only, the instrument of transfer is accompanied by the certificate of shares to which it relates (if any) and such other evidence as the directors may reasonably require to show the right of the transferor to make the transfer, the instrument of transfer is in favor of not more than four transferees and it is lodged at our registered office or such other place as our directors or secretary may appoint.

The directors may suspend registration of transfers from time to time, not exceeding 30 days in aggregate each year, as our board of directors may from time to time determine (except as may be required by law).

EXHIBIT 10.10

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY

RESTRICTED STOCK UNIT GRANT NOTICE
(2018 EQUITY INCENTIVE PLAN)

Iterum Therapeutics Public Limited Company (the "***Company***"), pursuant to its 2018 Equity Incentive Plan (the "***Plan***"), hereby awards to Participant the number of Restricted Stock Units set forth below (the "***Award***").

The Award is subject to all of the terms and conditions as set forth in this Restricted Stock Unit Grant Notice (this "***Grant Notice***") and the RSU Terms and Conditions (including Schedule 1) (collectively, the "***RSU Award Agreement***"), and the Plan, all of which are attached hereto and incorporated herein in their entirety. Capitalized terms not otherwise defined herein will have the meanings set forth in the Plan.

Participant:	_____
Date of Grant:	_____
Number of Restricted Stock Units:	_____

Vesting Schedule: The Restricted Stock Units shall vest, if at all, in accordance with the terms and conditions set forth on Schedule 1 to this RSU Award Agreement.

Issuance Schedule: The Ordinary Shares to be issued in respect of the Award will be issued in accordance with the issuance schedule set forth in Section 2 of the RSU Terms and Conditions.

Additional Terms/Acknowledgements: Participant acknowledges receipt of a copy of the Plan and represents that he or she is familiar with the terms and provisions thereof, and hereby accepts this Award subject to all of the terms and provisions of the Plan and this RSU Award Agreement. By accepting this Award, Participant acknowledges and agrees that Participant has reviewed the Plan and this RSU Award Agreement (including all attachments and exhibits) in its entirety. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Board or the Stock Plan Administrator upon any questions arising under the Plan or this Award.

Participant acknowledges and agrees that the RSU Award Agreement may not be modified, amended or revised except as provided in the PlanParticipant further acknowledges that as of the Date of Grant, this RSU Award Agreement and the Plan set forth the entire understanding between Participant and the Company regarding the acquisition of Ordinary Shares pursuant to the Award and supersede all prior oral and written agreements on that subject with the exception, if applicable, of (i) equity awards previously granted and delivered to Participant, (ii) any compensation recovery policy that is adopted by the Company or is otherwise required by applicable law, and (iii) any written employment or severance arrangement that would provide for vesting acceleration of this Award upon the terms and conditions set forth therein.

To facilitate the Award, Participant acknowledges that it may be necessary to receive documents by electronic delivery and to participate in the Plan through an on-line or electronic system established and maintained by the Company or a third party designated by the Company.

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY

By: _____
Signature

Title: _____

Date: _____

PARTICIPANT:

_____
Signature

Date: _____

Address/Country: _____

ATTACHMENTS:

Attachment I: RSU Terms and Conditions
Attachment II: 2018 Equity Incentive Plan

ATTACHMENT I

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY
2018 EQUITY INCENTIVE PLAN

RSU TERMS AND CONDITIONS

Iterum Therapeutics Public Limited Company (the "***Company***") has awarded you the number of Restricted Stock Units indicated in the Grant Notice (the "***Award***") pursuant to the Company's 2018 Equity Incentive Plan (the "***Plan***"). The Grant Notice, this RSU Terms and Conditions are collectively referred to as the "***RSU Award Agreement***". Capitalized terms not explicitly defined in the RSU Award Agreement will have the same meanings given to them in the Plan.

The terms of your Award, in addition to those set forth in the Grant Notice and the Plan, are as follows:

1. GRANT OF THE AWARD. This Award represents the right to be issued on a future date one (1) Ordinary Share for each Restricted Stock Unit that vests on the applicable vesting date(s) (subject to any adjustment under Section 3 below) as indicated in the Grant Notice. As of the Date of Grant, the Company will credit to a bookkeeping account maintained by the Company, or a third party designated by the Company, for your benefit (the "***Account***") the number of Restricted Stock Units/Ordinary Shares subject to the Award. Except as otherwise provided herein, you will not be required to make any payment to the Company or an Affiliate (other than services to the Company or an Affiliate) with respect to your receipt of the Award, the vesting of the Restricted Stock Units or the delivery of the Ordinary Shares to be issued in respect of the Award. Notwithstanding the foregoing, the Company reserves the right to issue you the cash equivalent of Ordinary Shares, in part or in full satisfaction of the delivery of Ordinary Shares upon vesting of your Restricted Stock Units, and, to the extent applicable, references in this RSU Award Agreement to Ordinary Shares issuable in connection with your Restricted Stock Units will include the potential issuance of its cash equivalent pursuant to such right, unless otherwise provided for your country in the Appendix.

2. VESTING. Subject to the limitations contained herein, your Award will vest, if at all, in accordance with the vesting schedule provided in the Grant Notice, provided that vesting will cease upon the termination of your Continuous Service. Upon such termination of your Continuous Service, the Restricted Stock Units/Ordinary Shares credited to the Account that were not vested on the date of such termination will be forfeited at no cost to the Company and you will have no further right, title or interest in or to such underlying Ordinary Shares.

For purposes of this Award, your Continuous Service will be considered terminated as of the date you are no longer actively providing services to the Company or an Affiliate (regardless of the reason for such termination and whether or not later found to be invalid or in breach of employment laws in the jurisdiction where you are employed or the terms of your employment agreement, if any), and unless otherwise expressly provided in the RSU Award Agreement or determined by the Company, (i) your right to vest in the Award, if any, will terminate as of such date and will not be extended by any notice period (that is your period of service would not include any contractual notice period or any period of "garden leave" or similar period mandated under employment laws in the jurisdiction where you are employed or the terms of your employment agreement, if any). The Board or its duly authorized designee shall have the exclusive discretion to determine when you are no longer actively providing services for purposes of your Award (including whether you may still be considered to be providing services while on a leave of absence).

The Ordinary Shares will be delivered to you as soon as practicable following each vesting date, but in any event within 30 days of such date.

3. NUMBER OF SHARES. The number of Restricted Stock Units/shares subject to your Award may be adjusted from time to time for Capitalization Adjustments, as provided in the Plan. Any additional Restricted Stock Units, shares, cash or other property that become subject to the Award pursuant to this Section 3, if any, will be subject, in a manner determined by the Board, to the same forfeiture restrictions, restrictions on transferability, and time and manner of delivery as applicable to the other Restricted Stock Units and shares covered by your Award.

4. Compliance with Law. You may not be issued any Ordinary Shares under your Award unless the Ordinary Shares underlying the Restricted Stock Units are either (i) then registered under the Securities Act, or (ii) the Company has determined that such issuance would be exempt from the registration requirements of the Securities Act. Your Award must also comply with other applicable laws and regulations governing the Award, including any U.S. and non-U.S. state, federal and local laws, and you will not receive such Ordinary Shares if the Company determines that such receipt would not be in material compliance with such laws and regulations.

5. Transfer Restrictions. Prior to the time that Ordinary Shares have been delivered to you, you may not transfer, pledge, sell or otherwise dispose of this Award or the shares issuable in respect of your Award, except as expressly provided in this Section 5. For example, you may not use shares that may be issued in respect of your Restricted Stock Units as security for a loan. The restrictions on transfer set forth herein will lapse upon delivery to you of shares in respect of your vested Restricted Stock Units. Notwithstanding the foregoing, by delivering written notice to the Company, in a form satisfactory to the Company, you may designate a third party who, in the event of your death, will thereafter be entitled to receive any distribution of Ordinary Shares to which you were entitled at the time of your death pursuant to this RSU Award Agreement. In the absence of such a designation, your legal representative will be entitled to receive, on behalf of your estate, such Ordinary Shares or other consideration to the extent applicable in accordance with your will or the laws of intestacy.

6. Dividends. You will receive no benefit or adjustment to your Award with respect to any cash dividend, stock dividend or other distribution that does not result from a Capitalization Adjustment; provided, however, that this sentence will not apply with respect to any Ordinary Shares that are delivered to you in connection with your Award after such shares have been delivered to you.

7. Unsecured Obligation. Your Award is unfunded, and as a holder of a vested Award, you will be considered an unsecured creditor of the Company with respect to the Company's obligation, if any, to issue shares or other property pursuant to this RSU Award Agreement. You will not have voting or any other rights as a stockholder of the Company with respect to the shares to be issued pursuant to this RSU Award Agreement until such shares are issued to you pursuant to Section 6 of this RSU Terms and Conditions. Upon such issuance, you will obtain full voting and other rights as a stockholder of the Company. Nothing contained in this RSU Award Agreement, and no action taken pursuant to its provisions, will create or be construed to create a trust of any kind or a fiduciary relationship between you and the Company or any other person.

8. Award not a Service Contract. Your Continuous Service with the Company, the Employer or any other Affiliate is not for any specified term and may be terminated by you or by the Company, the Employer or any other Affiliate at any time, for any reason, with or without cause and with or without notice. Nothing in this RSU Award Agreement (including, but not limited to, the vesting of your Award or the issuance of the shares subject to your Award), the Plan or any covenant of good faith and fair dealing that may be found implicit in this RSU Award Agreement or the Plan will: (i) confer upon you any right to continue in the employ of, or affiliation with the Employer; (ii) constitute any promise or commitment by the Company, the Employer or any other Affiliate regarding the fact or nature of future positions, future work assignments, future compensation or any other term or condition of employment or affiliation; (iii) confer any right or benefit under this RSU Award Agreement or the Plan unless such right or benefit has specifically accrued under the terms of this RSU Award Agreement or Plan; or (iv) deprive the Company or the Employer of the right to terminate you at any time and without regard to any future vesting opportunity that you may have. The grant of the Award shall not be interpreted as forming an employment or service contract with the Company. Under no circumstances on ceasing to be in employment or service of the Company will you be entitled to any compensation for any loss of any right or benefit or prospective right or benefit under the Plan which you might otherwise have enjoyed whether such compensation is claimed by way of damages for wrongful dismissal or other breach of contract or by way of compensation for loss of office or otherwise howsoever.

9. Responsibility for Taxes.

(a) You acknowledge that, regardless of any action taken by the Company or, if different, your employer (the "***Employer***") the ultimate liability for all income tax, social insurance, payroll tax, fringe benefit tax, payment on account or other tax related items related to your participation in the Plan and legally applicable to you ("***Tax-Related Items***") is and remains your responsibility and may exceed the amount actually withheld by the Company or

the Employer. You further acknowledge that the Company and the Employer (i) make no representations or undertakings regarding the treatment of any Tax-Related Items in connection with any aspect of your Restricted Stock Units, including, but not limited to, the grant of the Restricted Stock Units, the vesting and settlement of the Restricted Stock Units, the delivery or sale of any Ordinary Shares and the receipt of any dividends, and (ii) do not commit to and are under no obligation to structure the terms of the grant or any aspect of your Award to reduce or eliminate your liability for Tax-Related Items or achieve any particular tax result. Further, if you are subject to Tax-Related Items in more than one jurisdiction between the Date of Grant and the date of any relevant taxable or tax withholding event, as applicable, you acknowledge that the Company and/or the Employer (or former employer if applicable) may be required to withhold or account for Tax-Related Items in more than one jurisdiction.

(b) You acknowledge and agree that the Company has the right to deduct from payments of any kind otherwise due to you any federal, state, local or other taxes of any kind required by law to be withheld with respect to the grant, vesting or settlement of the RSUs. At such time as you are not aware of any material nonpublic information about the Company or the Ordinary Shares and you are not subject to any restriction on trading activities with respect to the Ordinary Shares pursuant to any Company insider trading or other policy, you shall execute the instructions set forth in Schedule 2 attached hereto (the "Automatic Sale Instructions") as the means of satisfying such tax obligation. If you do not execute the Automatic Sale Instructions prior to an applicable vesting date, then you agree that if under applicable law you will owe taxes at such vesting date on the portion of the award then vested the Company shall be entitled to immediate payment from you of the amount of any tax required to be withheld by the Company. The Company shall not deliver any Ordinary Shares to you until it is satisfied that all required withholdings have been made.

10. No Advice Regarding Grant. The Company is not providing any tax, legal or financial advice, nor is the Company making any recommendations regarding your participation in the Plan, or your acquisition or sale of the underlying Ordinary Shares. You are hereby advised to consult with your own personal tax, legal and financial advisors regarding your participation in the Plan before taking any action related to the Plan.

11. Notices. Any notices provided for in this Award Agreement or the Plan will be given in writing (including electronically) and will be deemed effectively given when personally delivered, when sent by fax or electronic mail (transmission confirmed), when actually delivered if sent express overnight courier service or five days after deposit in first class mail, postage prepaid, addressed to you at the last address you provided to the Company. The Company may, in its sole discretion, decide to deliver any documents related to participation in the Plan and this Award by electronic means or to request your consent to participate in the Plan by electronic means.

12. Governing Plan Document. Your Award is subject to all the provisions of the Plan, the provisions of which are hereby made a part of your Award, and is further subject to all interpretations, amendments, rules and regulations which may from time to time be promulgated and adopted pursuant to the Plan. If there is any conflict between the provisions of this RSU Award Agreement and the Plan, the terms of the Plan will control. In addition, your Award (and any compensation paid or shares issued under your Award) is subject to recoupment in accordance with The U.S. Dodd–Frank Wall Street Reform and Consumer Protection Act and any implementing regulations thereunder, any clawback policy adopted by the Company and any compensation recovery policy otherwise required by applicable law. No recovery of compensation under such a clawback policy will be an event giving rise to a right to voluntarily terminate employment upon a resignation for "good reason," or for a "constructive termination" or any similar term under any plan of or agreement with the Company.

13. Severability. If all or any part of this RSU Award Agreement or the Plan is declared by any court or governmental authority to be unlawful or invalid, such unlawfulness or invalidity will not invalidate any portion of this RSU Award Agreement or the Plan not declared to be unlawful or invalid. Any Section of this RSU Award Agreement (or part of such a Section) so declared to be unlawful or invalid will, if possible, be construed in a manner which will give effect to the terms of such Section or part of a Section to the fullest extent possible while remaining lawful and valid.

14. Waiver. You acknowledge that a waiver by the Company of breach of any provision of this RSU Award Agreement shall not operate or be construed as a waiver of any other provision of this RSU Award Agreement, or of any subsequent breach of this RSU Award Agreement.

15. Successors and Assigns. The rights and obligations of the Company under your Award will be transferable by the Company to any one or more persons or entities, and all covenants and agreements hereunder will inure to the benefit of, and be enforceable by, the Company's successors and assigns. All obligations of the Company under the Plan and this RSU Award Agreement will be binding on any successor to the Company, whether the existence of such successor is the result of a direct or indirect purchase, merger, consolidation, or otherwise, of all or substantially all of the business and assets of the Company.

16. Imposition of Other Requirements. The Company reserves the right to impose other requirements on your participation in the Plan, and on any Ordinary Shares acquired under the Plan, to the extent the Company determines it is necessary or advisable for legal or administrative reasons, and to require you to sign any additional agreements or undertakings that may be necessary to accomplish the foregoing. You agree upon request to execute any further documents or instruments necessary or desirable in the sole determination of the Company to carry out the purposes or intent of your Award.

17. Governing Law. The interpretation, performance and enforcement of this RSU Award Agreement will be governed by and construed in accordance with the Irish Companies Act 2014 (as same may be amended, replaced and/or consolidated in the future) as to matters within the scope thereof, and as to all other matters shall be governed by and construed in accordance with the internal laws of the State of Delaware, without regard to its principles of conflicts of laws.

18. Language. If you have received this RSU Award Agreement, or any other document related to this Award and/or the Plan translated into a language other than English and if the meaning of the translated version is different than the English version, the English version will control.

19. Insider Trading Restrictions/Market Abuse Laws. You acknowledge that you may be subject to insider trading restrictions and/or market abuse laws in applicable jurisdictions, including the United States and your country of residence, which may affect your ability to acquire or sell the Ordinary Shares or rights to the Ordinary Shares under the Plan during such times as you are considered to have "inside information" regarding the Company (as defined by the laws in your country). Any restrictions under these laws or regulations are separate from and in addition to any restrictions that may be imposed under any applicable Company insider trading policy. You acknowledge that it is your responsibility to comply with any applicable restrictions, and you are advised to speak to your personal advisor on this matter.

20. Foreign Asset/Account and Tax Reporting, Exchange Controls. Your country may have certain foreign asset, account and/or tax reporting requirements and exchange controls which may affect your ability to acquire or hold Ordinary Shares under the Plan or cash received from participating in the Plan (including from any dividends received or sale proceeds arising from the sale of Ordinary Shares) in a brokerage or bank account outside your country. You understand that you may be required to report such accounts, assets or transactions to the tax or other authorities in your country. You also may be required to repatriate sale proceeds or other funds received as a result of participation in the Plan to your country through a designated bank or broker and/or within a certain time after receipt. In addition, you may be subject to tax payment and/or reporting obligations in connection with any income realized under the Plan and/or from the sale of Ordinary Shares. You acknowledge that you are responsible for complying with all such requirements, and that you should consult personal legal and tax advisors, as applicable, to ensure compliance.

21. [intentionally left blank]

22. Nature of Grant. In accepting your Award, you acknowledge, understand and agree that:

(a) Participation in the Plan is voluntary and therefore you must accept the terms and conditions of the Plan and this Award as a condition to participating in the Plan and receipt of this Award. The Plan is discretionary in nature and the Company can amend, cancel, or terminate it at any time

(b) This Award and any other awards under the Plan are voluntary and occasional and do not create any contractual or other right to receive future awards or other benefits in lieu of future awards, even if similar awards have been granted repeatedly in the past. All determinations with respect to any such future awards, including, but

not limited to, the time or times when such awards are made, the size of such awards and performance and other conditions applied to the awards, will be at the sole discretion of the Company.

* * *

This RSU Terms and Conditions will be deemed to be accepted by you upon the signing by you or otherwise by your acceptance of the Grant Notice to which it is attached.

Schedule 1

Vesting Conditions

Participant's Restricted Stock Units shall vest in accordance with the following schedule, if at all, following the achievement of the First and Second Milestones (described below) (together, the "Performance Conditions"), provided that the Participant continues to be in Continuous Service on the date of achievement of each of the First and Second Milestone, as applicable (the "Service Condition").

Performance Conditions

Participant's Restricted Stock Units shall vest in the following proportions:

(a) 50% upon Board certification of the acceptance by the United States Food and Drug Administration (the "FDA") of a New Drug Application (or any successor form or application having substantially the same effect with respect to the approval of a drug for marketing and sale) for sulopenem (the "NDA"), provided such event occurs on or before December 31, 2021 (the "First Milestone"); and

(b) 50% on the date which is the initial deadline set by the FDA to complete its review of the NDA in accordance with the Prescription Drug User Fee Act, as certified by the Board, provided such event occurs on or before December 31, 2021 (the "Second Milestone").

For the avoidance of doubt, if Participant does not satisfy the Service Condition then any portion of the Restricted Stock Unit Award which has not vested will terminate and be canceled and Participant shall have no further rights with respect thereto. To the extent that the First and/or Second Milestone is not achieved on or before December 31, 2021, the portion of the Restricted Stock Units eligible to vest on achievement of such Milestone shall be immediately and automatically forfeited as of 11:59 pm CT on December 31, 2021.

For the avoidance of doubt, the term "Board" as used in this Schedule 1 shall refer to the Company's Board of Directors or its duly authorized designee, in accordance with the terms of the Plan.

Schedule 2

Automatic Sale Instructions

The undersigned hereby consents and agrees that any taxes due on a vesting date as a result of the vesting of Restricted Stock Units on such date shall be paid through an automatic sale of shares as follows:

(a) Upon any vesting of Restricted Stock Units pursuant to Section 2 hereof, the Company shall arrange for the sale of such number of Ordinary Shares issuable with respect to the Restricted Stock Units that vest pursuant to Section 2 as is sufficient to generate net proceeds sufficient to satisfy the Company's minimum statutory withholding obligations with respect to the income recognized by you upon the vesting of the Restricted Stock Units (based on minimum statutory withholding rates for all tax purposes, including payroll and social taxes, that are applicable to such income) or, if higher, the specified percentage of the Ordinary Shares set forth below, and the net proceeds of such sale shall be delivered to the Company to the extent necessary to satisfy the Company's tax withholding obligations and shall otherwise be delivered to you.

(b) You hereby appoint the Chief Executive Officer and the Chief Financial Officer, and any of them acting alone and with full power of substitution, to serve as your attorneys in fact to arrange for the sale of your Ordinary Shares in accordance with this Schedule 2. You agree to execute and deliver such documents, instruments and certificates as may reasonably be required in connection with the sale of the shares pursuant to this Schedule 2.

(c) You represent to the Company that, as of the date hereof, you are not aware of any material nonpublic information about the Company or the Ordinary Shares and are not subject to any restriction on trading activities with respect to the Ordinary Shares pursuant to any Company insider trading policy or other policy. You and the Company have structured this Agreement, including this Schedule 2, to constitute a "binding contract" relating to the sale of Ordinary Shares, consistent with the affirmative defense to liability under Section 10(b) of the Securities Exchange Act of 1934 under Rule 10b5-1(c) promulgated under such Act.

The Company shall not deliver any Ordinary Shares to you until it is satisfied that all required withholdings have been made.

Portion of Ordinary Shares to Be Sold Pursuant to these Automatic Sale Instructions

_____: Statutory Minimum Withholding Amount

OR IF HIGHER

_____% of the Ordinary Shares to be Issued With Respect to the Vesting of the Restricted Stock Award on such Vesting Date

_____

Participant Name: _____

Date: _____

EXHIBIT 10.10

ATTACHMENT II

2018 EQUITY INCENTIVE PLAN

EXHIBIT 10.26

INVESTOR RIGHTS AGREEMENT

This INVESTOR RIGHTS AGREEMENT (this "Agreement") is made and entered into as of January 21, 2020 by and among Iterum Therapeutics Bermuda Limited, a company formed under the laws of Bermuda (the "Company"), Iterum Therapeutics plc, an Irish public limited company ("Iterum"), including as guarantor, Iterum Therapeutics International Limited, a company formed under the laws of Ireland, as guarantor, Iterum Therapeutics US Limited, a company formed under the laws of Delaware, as guarantor, and Iterum Therapeutics US Holding Limited, a company formed under the laws of Delaware, as guarantor (the guarantors other than Iterum, collectively, the "Subsidiary Guarantors" and, together with Iterum, the "Guarantors") and the "Purchasers" named in that certain Securities Purchase Agreement by and among the Company, the Guarantors and the Purchasers dated as of January 16, 2020 (the "Purchase Agreement"). Capitalized terms used herein have the respective meanings ascribed thereto in the Purchase Agreement unless otherwise defined herein.

The parties hereby agree as follows:

1. Certain Definitions.

As used in this Agreement, the following terms shall have the following meanings:

"Applicable Percentage" means, with respect to any person on any date of determination, the quotient, expressed as a percentage, determined by dividing (i) the number of Ordinary Shares owned (directly or indirectly) by such person determined on a Fully Diluted Basis by (ii) the total number of Ordinary Shares that are issued and outstanding determined on a Fully Diluted Basis.

"Board" means the board of directors of Iterum.

"Closing Date" means the date of the purchase and sale of Units consisting of the Notes and the RLNs pursuant to the Purchase Agreement.

"Exchange Act" means the Securities Exchange Act of 1934, as amended, including the rules and regulations promulgated thereunder.

"Exchange Shares" means Ordinary Shares issued or issuable upon the exchange of the Notes pursuant to the terms thereof.

"Exempted Securities" means

(i) Ordinary Shares (or options or other rights to acquire Ordinary Shares or securities convertible or exchangeable into or exercisable for Ordinary Shares) issued pursuant to the Rights Offering;

(ii) Ordinary Shares (or options or other rights to acquire Ordinary Shares or securities convertible or exchangeable into or exercisable for Ordinary Shares) issued as a dividend or distribution on the Notes;

(iii) Ordinary Shares (or options or other rights to acquire Ordinary Shares or securities convertible or exchangeable into or exercisable for Ordinary Shares) issued by reason of a dividend, stock split, split-up or other distribution of Ordinary Shares, subject to compliance with the terms of the Indenture;

(iv) Ordinary Shares or options or other rights to acquire Ordinary Shares issued to employees or directors of, or consultants or advisors to Iterum or any of its Subsidiaries pursuant to a plan, agreement or arrangement approved by the Board or an authorized committee thereof (including, for the avoidance of doubt and without limitation, any Ordinary Shares or options or other rights to acquire Ordinary Shares issued pursuant to Iterum's 2015 Equity Incentive Plan and 2018 Equity Incentive Plan and any inducement grants made by Iterum pursuant to Nasdaq Listing Rule 5635(c)(4));

(v) Ordinary Shares (or options or other rights to acquire Ordinary Shares or securities convertible or exchangeable into or exercisable for Ordinary Shares) actually issued upon the exercise of options or other rights or upon the conversion or exchange of securities convertible or exchangeable into Ordinary Shares (including the Notes), in each case provided such issuance is pursuant to the terms of such option, right or other security;

(vi) Ordinary Shares (or options or other rights to acquire Ordinary Shares or securities convertible or exchangeable into or exercisable for Ordinary Shares) issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction;

(vii) Ordinary Shares (or options or other rights to acquire Ordinary Shares or securities convertible or exchangeable into or exercisable for Ordinary Shares) issued to suppliers or third-party service providers in connection with the provision of goods or services pursuant to transactions with such third parties or their Affiliates;

(viii) Ordinary Shares (or options or other rights to acquire Ordinary Shares or securities convertible or exchangeable into or exercisable for Ordinary Shares) issued in connection with sponsored research, collaboration, technology license, development, manufacturing, supply, distribution, marketing or other similar commercial agreements or strategic partnerships; or

(ix) Ordinary Shares (or options or other rights to acquire Ordinary Shares or securities convertible or exchangeable into or exercisable for Ordinary Shares) issued as acquisition consideration (but not in connection with a financing) pursuant to the acquisition of another entity by Iterum or any Guarantor by merger or the purchase of substantially all of the assets, the acquisition of assets of another entity by Iterum or any Guarantor, or other reorganization or to a joint venture agreement, provided that such issuances are approved by the Board and made in compliance with the Indenture.

"Force Majeure" means any unusual event arising from causes reasonably beyond the control of the Company or the Guarantors (or any person acting on their behalf), which by its nature could not have been foreseen by the Company or the Guarantors, or, if it could have been foreseen, was unavoidable, and which causes a delay in or prevents the performance of any

obligation of the Company and the Guarantors under this Agreement, including but not limited to, acts of God, fire, war, explosions, lightning, extreme weather conditions, power failure or surges, government shutdown, terrorism, insurrection, civil disturbance, strikes or other labor disputes, or restraint by court order or order of public authority or any other cause similar to the foregoing.

"Fully Diluted Basis" means the number of Ordinary Shares outstanding or held (as the case may be), assuming the conversion, exchange or exercise of all securities or other instruments or rights that are convertible into or exercisable or exchangeable for Ordinary Shares that are outstanding. For purposes of this definition, all Notes shall be deemed exchanged on the date of determination using the Physical Settlement (as defined in the Indenture).

"Governmental Entity" means any federal, state, local, foreign, international or multinational entity or authority exercising executive, legislative, judicial, regulatory, administrative or taxing functions of or pertaining to government.

"Indenture" means the indenture, dated as of the Closing Date, among the Company, Iterum, the Subsidiary Guarantors and U.S. Bank National Association, as trustee, under which the Notes are to be issued.

"Major Investors" means Sarissa Capital Offshore Master Fund LP, Sarissa Capital Catapult Fund LLC and Sarissa Capital Hawkeye Fund LP, and their respective successors.

"New Securities" means, collectively, equity securities of Iterum (including Ordinary Shares), whether or not currently authorized, as well as rights, options, or warrants to purchase such equity securities, or securities of any type whatsoever that are, or may become, convertible or exchangeable into or exercisable for such equity securities.

"Note" or "Notes" means the 6.500% Exchangeable Senior Subordinated Notes due 2025, fully and unconditionally guaranteed on an unsecured senior basis by Iterum, issued by the Company pursuant to the Purchase Agreement.

"Ordinary Shares" means the ordinary shares, $0.01 nominal value, of Iterum.

"Principal Amount" means, for any RLN, the Principal Amount set forth in such RLN (which shall be a Permitted Denomination (as defined in the RLN Indenture)).

"Principal Amount Multiple" means for any RLN, the product of the Principal Amount and 100.

"Prospectus" means (i) the prospectus included in any Registration Statement, as amended or supplemented by any prospectus supplement, with respect to the terms of the offering of any portion of the Registrable Securities covered by such Registration Statement and by all other amendments and supplements to the prospectus, including post-effective amendments and all material incorporated by reference in such prospectus, and (ii) any "free writing prospectus" as defined in Rule 405 under the Securities Act.

"Purchasers" means (i) the Purchasers identified in the Purchase Agreement and (ii) any permitted transferee of any Purchaser who is a subsequent holder of Registrable Securities.

"Register," "registered" and "registration" refer to a registration made by preparing and filing a Registration Statement or similar document in compliance with the Securities Act, and the declaration or ordering of effectiveness of such Registration Statement or document.

"Registration Default" shall mean, subject to the third sentence of Section 2(a), the occurrence of any of the following: (i) the Company and the Guarantors fail to file and/or make effective a Registration Statement covering the resale of all of the Registrable Securities in accordance with the timing and other requirements set forth in Section 2(a) or (ii) if a Registration Statement filed pursuant to Section 2(a) has been declared effective and such Registration Statement ceases to be effective or the prospectus contained therein ceases to be usable for resales of Registrable Securities (a) for more than sixty (60) consecutive days during the required effectiveness period or (b) for more than one hundred twenty (120) days (whether or not consecutive) in any 12-month period during the required effectiveness period. Notwithstanding the foregoing, any day on which a Force Majeure has occurred or is continuing shall not count toward the timing requirements for the filing of a Registration Statement under clause (i) above or the calculation of the number of days in clauses (ii)(a) and (b) above.

"Registrable Securities" means (A) in the case of a Registration Statement on Form S-1 (i) the Notes, (ii) the Exchange Shares, (iii) the RLNs, and (iv) any other securities issued or issuable with respect to or in exchange for the Notes, the Exchange Shares or the RLNs, whether by merger, charter amendment or otherwise and (B) in the case of a Registration Statement on Form S-3, the Exchange Shares; provided that a security shall cease to be a Registrable Security upon the earlier of (A) a sale pursuant to a Registration Statement, and (B) such security becoming eligible for sale without restriction by a Purchaser pursuant to Rule 144 and without the requirement to be in compliance with Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act.

"Registration Statement" means any registration statement of Iterum, the Company and the Subsidiary Guarantors under the Securities Act that covers the resale of any of the Registrable Securities pursuant to the provisions of this Agreement, amendments and supplements to such Registration Statement, including post-effective amendments, all exhibits and all material incorporated by reference in such Registration Statement.

"Registration Trigger " means the later of (i) the earlier of (x) the consummation of the Rights Offering and (y) the date that is one year following the Closing Date and (ii) the date on which the number of unissued Ordinary Shares that are available for issuance by Iterum, less the number of shares that are issuable upon exercise, conversion or exchange of outstanding options, warrants or other securities or that are reserved under any equity incentive plan maintained by Iterum or reserved for exchange of any Notes issued pursuant to the Rights Offering, is greater than the total number of Ordinary Shares that are issuable upon exchange of the then-outstanding Notes that were issued to the Purchasers pursuant to the Purchase Agreement on the Closing Date (disregarding any limitations on exchange in Section 14.01(c) of the Indenture).

"Required Purchasers" means, at any time, Purchasers holding Registrable Securities representing more than (a) 66 2/3 % of the aggregate principal amount of Notes that constitute Registrable Securities, and (b) 66 2/3% of the aggregate Principal Amount of RLNs that constitute Registrable Securities.

"Rights Offering" means any public offering of subscription rights to purchase Units consisting of Notes and RLNs by Iterum and the Company to holders of Ordinary Shares on a pro rata basis in accordance with their share ownership as of a record date to be determined by the board of directors of Iterum or a committee thereof. The Purchasers and their Affiliates shall not be entitled to purchase any Units pursuant to the Rights Offering (regardless of whether or not under Irish or other applicable law such subscription rights are required to be offered to the Purchasers).

"RLNs" means the limited recourse royalty-linked notes issued by the Company pursuant to the Purchase Agreement.

"RLN Indenture" means the Limited Recourse Royalty-Linked Notes Indenture, dated as of the Closing Date, by and among the Company, Iterum, the Subsidiary Guarantors, Iterum Holders' Representative LLC, as Holders' Representative, and Computershare Trust Company, N.A., as trustee.

"SEC" means the U.S. Securities and Exchange Commission.

"Securities Act" means the Securities Act of 1933, as amended, including the rules and regulations promulgated thereunder.

"Securityholder Questionnaire" has the meaning ascribed to such term in the Purchase Agreement.

"Shareholder Approval" means such approval as may be required from time to time by the applicable rules and regulations of the Nasdaq Stock Market (or any successor entity) from Iterum's shareholders with respect to the issuance of the Units (including the Notes) in connection with the sale to the Purchasers pursuant to the Purchase Agreement and/or the issuance of all Ordinary Shares issuable in connection with the exchange of any Notes issued to the Purchasers pursuant to the Purchase Agreement.

2. Registration.

(a) Registration Statement. The Company and the Guarantors shall use their best efforts to (i) promptly prepare and file with the SEC an initial Registration Statement on Form S-1 covering the resale of all of the Registrable Securities within ten (10) Business Days after the Registration Trigger and make such Registration Statement become effective with the SEC within sixty (60) days after the Registration Trigger (or as soon as practicable thereafter), and (ii) prepare, file and make become effective a Registration Statement on Form S-3 for the resale of Registrable Securities to replace the initial Registration Statement required in clause (i) prior to the time that Iterum is no longer eligible to forward incorporate by reference into a Registration Statement on Form S-1, provided that Iterum satisfies the eligibility requirements of Form S-3 at such time. In the event that Iterum again becomes eligible to forward incorporate by reference into a Registration Statement on Form S-1 at any time, Iterum shall promptly prepare and file with the SEC a Registration Statement on Form S-1 covering the resale of any Registrable Securities that are not otherwise registered pursuant to an effective Registration Statement within thirty (30) Business Days of becoming eligible. For the avoidance of doubt (I) at any time there is an effective Registration Statement on Form S-3 and Iterum is not eligible to forward incorporate by reference

on Form S-1, Iterum shall not be obligated to prepare, file, make effective or maintain the effectiveness of a Registration Statement on Form S-1 and (II) at any time there is an effective Registration Statement on Form S-1 and Iterum is eligible to forward incorporate by reference into such Registration Statement, Iterum shall not be obligated to prepare, file, make effective or maintain the effectiveness of a Registration Statement on Form S-3. Subject to any SEC comments, such Registration Statements shall include the plan of distribution attached hereto as Exhibit A; provided, however, that no Purchaser shall be named as an "underwriter" in such Registration Statement without the Purchaser's prior written consent. Such Registration Statements also shall cover, to the extent allowable under the Securities Act and the rules promulgated thereunder (including Rule 416), such indeterminate number of additional Ordinary Shares resulting from share splits, bonus issue of shares or similar transactions with respect to the Registrable Securities. Such Registration Statements (and each amendment or supplement thereto, and each request for acceleration of effectiveness thereof) shall be provided in accordance with Section 3(c) hereof to the Purchasers prior to its filing or other submission.

(b) Expenses. The Company, Iterum and the Subsidiary Guarantors, other than Iterum Therapeutics International Limited, will pay all expenses associated with each Registration Statement, including (i) filing and printing fees, (ii) the Company's and the Guarantors' counsel and accounting fees and expenses, (iii) costs associated with clearing the Registrable Securities for sale under applicable state securities laws and listing fees, and (iv) all rating agency fees incurred by the Company or the Guarantors (including with respect to maintaining ratings of the Notes and/or the RLNs), but excluding discounts, commissions, fees of underwriters, selling brokers, dealer managers or similar securities industry professionals with respect to the Registrable Securities being sold.

(c) Effectiveness.

(i) The Company and the Guarantors shall use their best efforts to have each Registration Statement declared effective as soon as practicable after such Registration Statement is filed with the SEC. The Company or a Guarantor shall notify the Purchasers by facsimile or e-mail as promptly as practicable, and in any event, within twenty-four (24) hours, after any Registration Statement is declared effective and shall simultaneously provide the Purchasers with copies of any related Prospectus to be used in connection with the sale or other disposition of the securities covered thereby.

(ii) For not more than sixty (60) consecutive days or for a total of not more than one hundred twenty (120) days in any twelve (12) month period, the Company or Iterum may suspend the use of any Prospectus included in any Registration Statement contemplated by this Section 2 in the event that the Company or Iterum determines in good faith that such suspension is necessary to (A) delay the disclosure of material non-public information concerning the Company or Iterum, the disclosure of which at the time is not, in the good faith opinion of the Company or Iterum, in the best interests of the Company or Iterum, (B) amend or supplement the affected Registration Statement or the related Prospectus so that such Registration Statement or Prospectus shall not include an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in the case of the Prospectus in light of the circumstances under which they were made, not misleading, (C) permit the Company or Iterum to conduct a sale of securities or other financing that is not a sale of

Registrable Securities or (D) file a replacement Registration Statement covering the resale of Registrable Securities in connection with the expiration or anticipated expiration of an effective Registration Statement (an "Allowed Delay"); provided that the Company or Iterum shall promptly (a) notify each Purchaser in writing of the commencement of an Allowed Delay, but shall not (without the prior written consent of a Purchaser) disclose to such Purchaser any material non-public information giving rise to an Allowed Delay, (b) advise the Purchasers in writing to cease all sales under such Registration Statement until the end of the Allowed Delay and (c) use best efforts to terminate an Allowed Delay as promptly as practicable.

(d) Rule 415; Cutback. If at any time the SEC takes the position that the offering of some or all of the Registrable Securities in a Registration Statement is not eligible to be made on a delayed or continuous basis under the provisions of Rule 415 under the Securities Act or requires any Purchaser to be named as an "underwriter," the Company and the Guarantors shall use their best efforts to persuade the SEC that the offering contemplated by such Registration Statement is a valid secondary offering and not an offering "by or on behalf of the issuer" as defined in Rule 415 and that none of the Purchasers is an "underwriter." The Purchasers shall have the right to select one legal counsel to review and oversee any registration or matters pursuant to this Section 2(d), including participation in any meetings or discussions with the SEC regarding the SEC's position and to comment on any written submission made to the SEC with respect thereto, which counsel shall be designated by the Required Purchasers. In the event that, despite the Company's and the Guarantors' best efforts and compliance with the terms of this Section 2(d), the SEC does not alter its position, the Company and the Guarantors shall (i) remove from such Registration Statement such portion of the Registrable Securities (the "Cut Back Securities") and/or (ii) agree to such restrictions and limitations on the registration and resale of the Registrable Securities as the SEC may require to assure the Company's and the Guarantors' compliance with the requirements of Rule 415 (collectively, the "SEC Restrictions"); provided, however, that the Company and the Guarantors shall not agree to name any Purchaser as an "underwriter" in such Registration Statement without the prior written consent of such Purchaser. Any cut-back imposed on the Purchasers pursuant to this Section 2(d) shall be allocated among the Purchasers on a pro rata basis and shall be applied first to any of the Registrable Securities of such Purchaser as such Purchaser shall designate, unless the SEC Restrictions otherwise require or provide or the Purchasers otherwise agree. From and after such date as the Company and the Guarantors are able to effect the registration of such Cut Back Securities, the Company and the Guarantors shall use their best efforts to file a Registration Statement relating to such Cut Back Securities and to have such Registration Statement declared effective by the SEC.

(e) Registration Default.

(i) If a Registration Default occurs, then (i) with respect to Registrable Securities that constitute Notes, the interest rate on such Notes will be increased by (A) 0.25% per annum for the first 90-day period beginning on the day immediately following such Registration Default and (B) an additional 0.25% per annum with respect to each subsequent 90-day period, in each case until and including the date such Registration Default ends, up to a maximum increase of 1.00% per annum and (ii) with respect to Registrable Securities that constitute RLNs, interest will accrue at (A) 0.25% per annum on the Principal Amount Multiple of such RLNs for the first 90-day period beginning on the day immediately following such Registration Default and (B) an additional 0.25% per annum with respect to each subsequent 90-day period, in each case until and

including the date such Registration Default ends, up to a maximum of 1.00% per annum, and such interest shall become due and payable on the first Interest Payment Date (as such term is defined in the RLN Indenture) to occur after the occurrence of such Registration Default, and on each Interest Payment Date thereafter that corresponds to any Interest Measuring Period (as such term is defined in the RLN Indenture) during which such Registration Default shall be continuing. A Registration Default ends with respect to any security when such security ceases to be a Registrable Security or, if earlier, (1) in the case of a Registration Default under clause (i) of the definition thereof, when a Registration Statement filed pursuant to Section 2(a) becomes effective or (2) in the case of a Registration Default under clause (ii) of the definition thereof, when such Registration Statement again becomes effective or such Prospectus again becomes usable. If at any time more than one Registration Default has occurred and is continuing, then, until the next date that there is no Registration Default, the increase in interest rate provided for by this paragraph shall apply as if there occurred a single Registration Default that begins on the date that the earliest such Registration Default occurred and ends on the next date that there is no Registration Default.

(ii) Without limiting the remedies available to the Purchasers, the Company and the Guarantors acknowledge that any failure by the Company or the Guarantors to comply with their obligations under Section 2 hereof would result in material irreparable injury to the Purchasers for which there is no adequate remedy at law, that it will not be possible to measure damages for such injuries precisely and that, in the event of any such failure, the Purchasers may specifically enforce the Company's and the Guarantors' obligations under this Section 2 without the need to show actual damages and without the need to post a bond or other security.

3. Company and Guarantor Obligations. The Company and the Guarantors will use their best efforts to effect the registration of the Registrable Securities in accordance with the terms hereof, and pursuant thereto the Company and the Guarantors will:

(a) subject to the third sentence in Section 2(a), use their best efforts to cause such Registration Statement (including any additional or replacement Registration Statement) to remain continuously effective for a period that will terminate upon the earlier of (i) the date on which all Registrable Securities that are covered by such Registration Statement, as amended from time to time, and actually issued or issuable upon exchange of the Notes have been sold, (ii) the date on which all Registrable Securities that are covered by such Registration Statement and actually issued or issuable upon exchange of the Notes may be sold without restriction pursuant to Rule 144 and without the requirement to be in compliance with Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act and (iii) the date that is six years following the date the initial Registration Statement initially becomes effective (the "Effectiveness Period"), and advise the Purchasers promptly in writing when the Effectiveness Period has expired;

(b) use their best efforts to prepare and file with the SEC such amendments and post-effective amendments to each such Registration Statement and the related Prospectus as may be necessary to keep such Registration Statement effective for the Effectiveness Period and to comply with the provisions of the Securities Act and the Exchange Act with respect to the distribution of all of the Registrable Securities covered thereby;

(c) provide copies to and permit any counsel designated by the Required Purchasers to review each Registration Statement and all amendments and supplements thereto

(but excluding any documents incorporated by reference in such Registration Statement, amendments or supplements that are available on the SEC's Electronic Data Gathering, Analysis, and Retrieval system (or any successor system)) no fewer than three (3) Business Days prior to their filing with the SEC and not file any document to which such counsel reasonably objects;

(d) furnish to each Purchaser whose Registrable Securities are included in any Registration Statement (i) promptly after the same is prepared and filed with the SEC, if requested by the Purchaser, one (1) copy of any Registration Statement and any amendment thereto, each preliminary prospectus and Prospectus and each amendment or supplement thereto, and each letter written by or on behalf of the Company or the Guarantors to the SEC or the staff of the SEC, and each item of correspondence from the SEC or the staff of the SEC, in each case relating to such Registration Statement (other than any portion of any of the foregoing which contains information for which the Company or the Guarantors have sought confidential treatment), and (ii) such number of copies of a Prospectus, including a preliminary prospectus, and all amendments and supplements thereto and such other documents as each Purchaser may reasonably request in order to facilitate the disposition of the Registrable Securities owned by such Purchaser that are covered by such Registration Statement;

(e) use commercially reasonable efforts to (i) prevent the issuance of any stop order or other suspension of effectiveness and, (ii) if such order is issued, obtain the withdrawal of any such order at the earliest practical moment;

(f) prior to any public offering of Registrable Securities, use commercially reasonable efforts to register or qualify or cooperate with the Purchasers and their counsel in connection with the registration or qualification of such Registrable Securities for the offer and sale under the securities or blue sky laws of such jurisdictions requested by the Purchasers and do any and all other commercially reasonable acts or things necessary or advisable to enable the distribution in such jurisdictions of the Registrable Securities covered by the Registration Statement; provided, however, that the Company and the Guarantors shall not be required in connection therewith or as a condition thereto to (i) qualify to do business in any jurisdiction where it would not otherwise be required to qualify but for this Section 3(f), (ii) subject itself to general taxation in any jurisdiction where it would not otherwise be so subject but for this Section 3(f), or (iii) file a general consent to service of process in any such jurisdiction;

(g) use their best efforts to cause all Registrable Securities covered by a Registration Statement to be listed on each securities exchange, interdealer quotation system or other market on which similar securities issued by the Company or Iterum are then listed;

(h) promptly notify the Purchasers, at any time prior to the end of the Effectiveness Period, upon discovery that, or upon the happening of any event as a result of which, the Prospectus includes an untrue statement of a material fact or omits to state any material fact required to be stated therein or necessary to make the statements therein not misleading in light of the circumstances then existing, but shall not (without the prior written consent of a Purchaser) disclose to such Purchaser any other material non-public information, and promptly prepare, file with the SEC and furnish to such holder a supplement to or an amendment of such Prospectus as may be necessary so that such Prospectus shall not include an untrue statement of a material fact

or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading in light of the circumstances then existing;

(i) otherwise use their best efforts to comply with all applicable rules and regulations of the SEC under the Securities Act and the Exchange Act, including, without limitation, Rule 172 under the Securities Act, file any final Prospectus, including any supplement or amendment thereof, with the SEC pursuant to Rule 424 under the Securities Act, promptly inform the Purchasers in writing if, at any time during the Effectiveness Period, Iterum does not satisfy the conditions specified in Rule 172 and, as a result thereof, the Purchasers are required to deliver a Prospectus in connection with any disposition of Registrable Securities and take such other actions as may be reasonably necessary to facilitate the registration of the Registrable Securities hereunder; and make available to its security holders, as soon as reasonably practicable, an earnings statement covering a period of at least twelve (12) months, beginning after the effective date of each Registration Statement, which earnings statement shall satisfy the provisions of Section 11(a) of the Securities Act, including Rule 158 promulgated thereunder;

(j) with a view to making available to the Purchasers the benefits of Rule 144 (or its successor rule) and any other rule or regulation of the SEC that may at any time permit the Purchasers to sell securities to the public without registration, Iterum covenants and agrees to: (i) make and keep adequate current public information available, as those terms are understood and defined in Rule 144, until the earlier of (A) six months after such date as all of the Registrable Securities may be sold without restriction by the holders thereof pursuant to Rule 144 and without the requirement to be in compliance with Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act or any other rule of similar effect or (B) such date as all of the Registrable Securities shall have been resold; (ii) file with the SEC in a timely manner all reports and other documents required of Iterum under the Exchange Act; and (iii) furnish to each Purchaser upon request, as long as such Purchaser owns any Registrable Securities, (A) a written statement by Iterum that it has complied with the reporting requirements of the Exchange Act, (B) a copy of Iterum's most recent Annual Report on Form 10-K or Quarterly Report on Form 10-Q, and (C) such other information as may be reasonably requested in order to avail such Purchaser of any rule or regulation of the SEC that permits the selling of any such Registrable Securities without registration;

(k) make available at reasonable times at the Company or the Guarantors' principal place of business or such other reasonable place for inspection by the Purchasers, and any attorney or accountant retained by such Purchaser, all pertinent financial and other records and pertinent corporate documents of each of the Company and the Guarantors as may be reasonably necessary for the purpose of review as reasonably requested by the Purchasers and cause the Company's and the Guarantors' officers, directors and employees to supply within a reasonable time period all information reasonably requested by any such Purchaser, attorney or accountant in connection with any Registration Statement or any post-effective amendment thereto subsequent to the filing thereof and prior to its effectiveness, as shall be reasonably necessary for the sole purpose of enabling such Persons to conduct an investigation within the meaning of Section 11 of the Securities Act; provided, however, that the conduct of the foregoing inspection shall be subject to the execution by all Persons party to such inspection of a reasonable confidentiality and non-use undertaking in customary form with respect to confidential and propriety information of the Company and the Guarantors; and

(l) not later than ten (10) Business Days following the date on which Shareholder Approval is obtained, provide a CUSIP number for all Registrable Securities.

4. Obligations of the Purchasers.

(a) It shall be a condition precedent to the obligations of the Company and the Guarantors to take any action pursuant to Section 2 hereof with respect to the Registrable Securities of any Purchaser that such Purchaser furnish in writing to the Company and the Guarantors a Securityholder Questionnaire and any other information regarding itself, the Registrable Securities held by it and the intended method of disposition of the Registrable Securities held by it, as shall be reasonably required to effect the registration of such Registrable Securities, and such Purchaser shall execute such documents in connection with such registration as the Company and the Guarantors may reasonably request. At least five (5) Business Days prior to the first anticipated filing date of any Registration Statement, the Company or the Guarantors shall notify each Purchaser of the information the Company and the Guarantors require from such Purchaser if such Purchaser elects to have any of the Registrable Securities included in such Registration Statement. A Purchaser shall provide such information to the Company and the Guarantors at least three (3) Business Days prior to the first anticipated filing date of such Registration Statement if such Purchaser elects to have any of the Registrable Securities included in such Registration Statement.

(b) Each Purchaser, by its acceptance of the Registrable Securities, agrees to cooperate with the Company and the Guarantors as reasonably requested by the Company and the Guarantors in connection with the preparation and filing of a Registration Statement hereunder, unless such Purchaser has notified the Company and the Guarantors in writing of its election to exclude all of its Registrable Securities from such Registration Statement.

(c) Each Purchaser agrees that, upon receipt of any notice from the Company or the Guarantors of either (i) the commencement of an Allowed Delay pursuant to Section 2(c)(ii) or (ii) the happening of an event pursuant to Section 3(h) hereof, such Purchaser will immediately discontinue disposition of Registrable Securities pursuant to any Registration Statement covering such Registrable Securities, until the Purchaser is advised by the Company or a Guarantor that such dispositions may again be made.

(d) Each Purchaser covenants and agrees that it will comply with the prospectus delivery requirements of the Securities Act as applicable to it or an exemption therefrom in connection with sales of Registrable Securities pursuant to any Registration Statement.

5. Indemnification.

(a) Indemnification by the Company and the Guarantors. The Company and the Guarantors, jointly and severally, will indemnify and hold harmless each Purchaser and its officers, directors, members, employees, investment advisers and agents, successors and assigns, and each other person, if any, who controls such Purchaser within the meaning of the Securities Act (the "Purchaser Indemnified Parties"), against any losses, claims, damages or liabilities, joint or several, to which they may become subject under the Securities Act or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon: (i) any untrue statement or alleged untrue statement or omission or alleged omission of any

material fact contained in any Registration Statement, any preliminary Prospectus or final Prospectus, or any amendment or supplement thereof; (ii) any violation by the Company or a Guarantor or their agents of any rule or regulation promulgated under the Securities Act applicable to the Company or a Guarantor or their agents and relating to action or inaction required of the Company or a Guarantor in connection with the performance of their obligations under this Agreement; or (iii) any failure to register or qualify the Registrable Securities included in any such Registration Statement in any state where the Company, a Guarantor or their agents have affirmatively undertaken or agreed in writing that the Company or a Guarantor, as applicable, will undertake such registration or qualification on a Purchaser's behalf, and will reimburse such Purchaser, and each such Purchaser Indemnified Party for any documented, out-of-pocket legal or other expenses reasonably incurred by them in connection with investigating or defending any such loss, claim, damage, liability or action; provided, however, that the Company and the Guarantors will not be liable in any such case if and to the extent that any such loss, claim, damage or liability arises out of or is based upon (i) an untrue statement or alleged untrue statement or omission or alleged omission so made in conformity with information furnished by such Purchaser or any such controlling person in writing specifically for use in such Registration Statement or Prospectus, (ii) the use by any Purchaser of an outdated or defective Prospectus after the Company or Iterum has notified such Purchaser in writing that such Prospectus is outdated or defective, (iii) a Purchaser's failure to send or give a copy of the Prospectus or supplement (as then amended or supplemented), if required (and not exempted) to the Persons asserting an untrue statement or omission or alleged untrue statement or omission at or prior to the written confirmation of the sale of Registrable Securities, (iv) a Purchaser's fraud or (v) the disposition of any Registrable Securities pursuant to any Registration Statement or Prospectus covering such Registrable Securities during an Allowed Delay.

(b) Indemnification by the Purchasers. Each Purchaser agrees, severally but not jointly, to indemnify and hold harmless, to the fullest extent permitted by law, the Company, the Guarantors, their respective directors, officers, employees, stockholders, shareholders and each person who controls the Company or a Guarantor (within the meaning of the Securities Act) against any losses, claims, damages, liabilities and expense (including reasonable attorney fees) resulting from any untrue statement of a material fact or any omission of a material fact required to be stated in any Registration Statement or Prospectus or preliminary Prospectus or amendment or supplement thereto or necessary to make the statements therein not misleading, to the extent, but only to the extent that such untrue statement or omission is made in conformity with any information furnished in writing by such Purchaser to the Company and the Guarantors specifically for inclusion in such Registration Statement or Prospectus or amendment or supplement thereto. Except to the extent that any such losses, claims, damages, liabilities or expenses are finally judicially determined to have resulted from a Purchaser's fraud, in no event shall the liability of a Purchaser be greater in amount than the dollar amount of the proceeds (net of all expense paid by such Purchaser in connection with any claim relating to this Section 5 and the amount of any damages such Purchaser has otherwise been required to pay by reason of such untrue statement or omission) received by such Purchaser upon the sale of the Registrable Securities included in such Registration Statement giving rise to such indemnification obligation.

(c) Conduct of Indemnification Proceedings. Any person entitled to indemnification hereunder shall (i) give prompt written notice to the indemnifying party of any claim with respect to which it seeks indemnification and (ii) permit such indemnifying party to

assume the defense of such claim with counsel reasonably satisfactory to the indemnified party; provided that any person entitled to indemnification hereunder shall have the right to employ separate counsel and to participate in the defense of such claim, but the fees and expenses of such counsel shall be at the expense of such person unless (a) the indemnifying party has agreed to pay such fees or expenses, (b) the indemnifying party shall have failed to assume the defense of such claim and employ counsel reasonably satisfactory to such person or (c) in the reasonable judgment of any such person, based upon written advice of its counsel, a conflict of interest exists between such person and the indemnifying party with respect to such claims (in which case, if the person notifies the indemnifying party in writing that such person elects to employ separate counsel at the expense of the indemnifying party, the indemnifying party shall not have the right to assume the defense of such claim on behalf of such person); and provided, further, that the failure of any indemnified party to give written notice as provided herein shall not relieve the indemnifying party of its obligations hereunder, except to the extent that such failure to give notice shall materially adversely affect the indemnifying party in the defense of any such claim or litigation. It is understood that the indemnifying party shall not, in connection with any proceeding in the same jurisdiction, be liable for fees or expenses of more than one separate firm of attorneys at any time for all such indemnified parties. No indemnifying party will, except with the consent of the indemnified party, which shall not be unreasonably withheld or conditioned, consent to entry of any judgment or enter into any settlement that does not include as an unconditional term thereof the giving by the claimant or plaintiff to such indemnified party of a release from all liability in respect of such claim or litigation.

(d) Contribution. If for any reason the indemnification provided for in the preceding paragraphs (a) and (b) is unavailable to an indemnified party or insufficient to hold it harmless, other than as expressly specified therein, then the indemnifying party shall contribute to the amount paid or payable by the indemnified party as a result of such loss, claim, damage or liability in such proportion as is appropriate to reflect the relative fault of the indemnified party and the indemnifying party, as well as any other relevant equitable considerations. No person guilty of fraudulent misrepresentation within the meaning of Section 11(f) of the Securities Act shall be entitled to contribution from any person not guilty of such fraudulent misrepresentation. Except to the extent that any such losses, claims, damages, liabilities or expenses are finally judicially determined to have resulted from the applicable holder of Registrable Securities' fraud, in no event shall the contribution obligation of a holder of Registrable Securities be greater in amount than the dollar amount of the proceeds (net of all expenses paid by such holder in connection with any claim relating to this Section 5 and the amount of any damages such holder has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission) received by it upon the sale of the Registrable Securities giving rise to such contribution obligation.

6. Pre-emptive Rights.

(a) Subject to the terms and conditions of this Section 6 and applicable securities or blue sky laws, if Iterum proposes to offer or sell any New Securities, Iterum shall first offer such New Securities to each Major Investor in accordance with the terms hereof. A Major Investor shall be entitled to apportion the right of first offer hereby granted to it in such proportions as it deems appropriate, among (i) itself and other Major Investors, (ii) its Affiliates and (iii) its beneficial interest holders, such as limited partners, members or any other Person having

"beneficial ownership," as such term is defined in Rule 13d-3 promulgated under the Exchange Act, of such Major Investor.

(b) Iterum shall give notice (the "Offer Notice") to each Major Investor, stating (i) its bona fide intention to offer or sell such New Securities, (ii) the number of such New Securities to be offered, and (iii) the price and terms, if any, upon which it proposes to offer such New Securities.

(c) By written notification to Iterum within thirty (30) days after the Offer Notice is delivered to a Major Investor, such Major Investor may elect to purchase or otherwise acquire, at the price and on the terms specified in the Offer Notice, up to that portion of such New Securities which equals the Major Investor's Applicable Percentage. The failure of any such Major Investor to deliver such written notice within such time period shall be deemed an election by such Major Investor not to exercise its purchase rights with respect to such Offer Notice. To the extent that Iterum offers two (2) or more New Securities or other securities in units, the Major Investors must purchase such units as a whole and will not be given the opportunity to purchase only one of the securities making up such unit.

(d) Iterum shall sell all applicable New Securities to electing Major Investors on a date to be mutually determined by Iterum and the Major Investors, which date shall be during the ten (10) day period commencing at the expiration of the initial thirty (30) day election period; provided, however, that such ten (10) day period shall be extended automatically if any approvals or consents of any Governmental Entities are required to consummate the transaction and such approvals or consents are not received within such ten (10) day period for up to an additional one hundred twenty (120) days as long as such approvals or consents remain outstanding and the parties are continuing to exercise commercially reasonable efforts to obtain them.

(e) Upon the expiration of the offering period described in Section 6(d), Iterum will be free to sell, during the one hundred twenty (120) day period commencing at the expiration of, as applicable, the initial thirty (30) day election period following delivery of an Offer Notice (as may be extended in accordance with Section 6(d)), any New Securities that the Major Investors have not elected to purchase, at a sale price not less than, and on other terms no less favorable to Iterum than, those offered to the Major Investors as set forth in the Offer Notice, provided, that such one hundred twenty (120) day period shall be extended automatically if any approvals or consents of any Governmental Entities are required to consummate the transaction and such approvals or consents are not received within such one hundred twenty (120) day period for up to an additional one hundred twenty (120) days as long as such approvals or consents remain outstanding and the parties are continuing to exercise commercially reasonable efforts to obtain them. Any New Securities offered or sold by Iterum after such one hundred twenty (120) day period (as such period may be extended in accordance with the immediately preceding sentence) must be reoffered to the Major Investors pursuant to this Section 6.

(f) The election by a Major Investor not to exercise its subscription rights under this Section 6 in any one instance shall not affect its right (other than in respect of a reduction in its Applicable Percentage) as to any subsequent proposed issuance of New Securities under this Section 6. The provisions of this Section 6 shall apply equally to any issuance or sale by the Company, any of the Guarantors or any of their controlled Affiliates of equity securities that would

be deemed New Securities if issued by Iterum which, for the avoidance of doubt, shall not include any issuance of New Securities by a wholly owned Subsidiary to its parent or to another wholly owned Subsidiary of such parent. Subject to the terms of this Section 6, any sale of New Securities by Iterum or any other entity covered by the preceding sentence without first giving the Major Investors the rights described in this Section 6 shall be null and void and of no force and effect.

(g) Notwithstanding the terms set forth in this Section 6, if the Board determines in good faith that Iterum must issue New Securities on an expedited basis without prior compliance with the terms of this Section 6 in order to avoid material harm to Iterum or any of its Affiliates (an "Expedited Issuance"), then, subject to compliance with the terms of the immediately following sentence, Iterum may effect and consummate such Expedited Issuance without complying with the terms set forth in this Section 6 and shall not be deemed to be in breach of this Section 6 as a result thereof. As promptly as practicable following the consummation of such Expedited Issuance, Iterum and the Major Investors shall comply with the terms of this Section 6 in respect of the New Securities issued in such Expedited Issuance such that all Major Investors have the opportunity to participate in such Expedited Issuance of New Securities and be put in the same place (including in respect of the percentage ownership of the equity securities of Iterum) they would have been had such Expedited Issuance been effected in accordance with the terms of this Section 6.

(h) Notwithstanding the terms set forth in this Section 6, Iterum may issue New Securities pursuant to the provisions of this Section 6(h) and without compliance with the other provisions of this Section 6 (each such transaction or series of related transactions, an "Excused Issuance"); provided that, in any twelve month period, without compliance with the other provisions of this Section 6, (A) the Company may not issue New Securities pursuant to the provisions of this Section 6(h) (other than Exempted Securities) which exceed (in the aggregate with all other Excused Issuances during such 12 month period) 5% of the issued and outstanding Ordinary Shares on a Fully Diluted Basis and (B) the Company may not issue New Securities pursuant to the provisions of this Section 6(h) (other than Exempted Securities) in exchange for consideration (whether in cash or other property) the value of which exceeds (in the aggregate with all other Excused Issuances during such 12 month period) $5,000,000. Notwithstanding the foregoing, the Company may only consummate two (2) Excused Issuances for so long as this Agreement is in effect.

(i) The provisions of this Section 6 (i) shall not apply to the issuance of Exempted Securities and (ii) shall terminate and be of no further force or effect as of such time that the Major Investors collectively, and together with their Affiliates, have an Applicable Percentage of less than 10%.

7. Board Matters.

(a) For so long as the Major Investors collectively, and together with their Affiliates, have an Applicable Percentage of at least 5%, in the case of the following clause (i)(x) in this sentence, and 12.5%, in the case of clause (i)(y) in this sentence: (i) promptly, and in any event no more than five (5) Business Days following the written request of the Major Investors, Iterum shall cause the Board to be expanded to consist of (x) nine (9) members or (y) ten (10) members (such number being sufficient to allow the Investor Designees to be appointed to the

Board pursuant to Section 7(b)) and (ii) Iterum shall cause the Board to consist of not more than ten (10) members without the prior written consent of the Major Investors (which shall not be unreasonably withheld). The obligation of Iterum to cause the Board to consist of not more than ten (10) members as provided in the immediately preceding sentence shall terminate and be of no further force or effect as of such time that the Major Investors collectively, and together with their Affiliates, have an Applicable Percentage of less than 5%.

(b) For so long as the Major Investors, collectively, and together with their Affiliates, have an Applicable Percentage of at least 12.5%, the Major Investors shall have the right to designate two (2) directors to the Board, and for so long as the Major Investors, collectively, and together with their Affiliates, continue to have an Applicable Percentage of at least 5% but less than 12.5%, the Major Investors shall have the right to designate one (1) director to the Board, in each case in accordance with the terms of this Section 7. Any directors designated by the Major Investors in accordance with this Section 7 shall be referred to as "Investor Designees". The right to designate one or more Investor Designees shall terminate and be of no further force or effect as of such time that the Major Investors collectively, and together with their Affiliates, have an Applicable Percentage of less than an applicable threshold percentage referenced in the first sentence of this Section 7(b). At any point in which the Major Investors are entitled to designate an Investor Designee, the Major Investors may provide written notice (a "Designation Notice") to Iterum naming the applicable Investor Designee(s) and demanding that the applicable Investor Designee(s) be appointed to the Board. Subject to subsections (i) and (j) of this Section 7, promptly, and in any event within five (5) Business Days, following receipt of the Designation Notice, Iterum shall cause the Investor Designees to be appointed to the Board and to be members of the class of directors for the purposes of Article 152 of Iterum's Constitution, which was subject to reelection at Iterum's most recent annual meeting of shareholders. Following the delivery of a Designation Notice and prior to the appointment of the Investor Designees to the Board, Iterum shall not (and shall cause its Subsidiaries not to) take or approve any action outside of the ordinary course of business including (without limitation) in respect of (i) strategic transactions, joint ventures and collaborations, (ii) the sale or acquisition of assets whether by merger, consolidation or otherwise, (iii) issuance of equity other than under employee incentive plans, (iv) incurrence or prepayment of debt, (v) declaration or payment of any dividend or distribution, or (vi) the initiation or suspension of any clinical trials. With respect to any vote of the Board, each director shall have one (1) vote and approval of all matters shall require the affirmative vote of a majority of directors.

(c) Subject to the terms of this Section 7, from and after the date hereof, Iterum shall take all action within its power to cause the covenants set forth in Section 7(a) and Section 7(b) to be fulfilled in all respects including: (i) causing the Investor Designees to be named in any proxy statement of Iterum with respect to the election of members of their relevant class of the Board, (ii) soliciting the votes of shareholders in respect of the Investor Designees in the same manner and with the same level of effort as with the solicitation in respect of other members of the Board, (iii) seeking to amend any organizational documents of Iterum necessary to give effect to the Major Investors' rights hereunder as may reasonably be requested by the Major Investors and (iv) take all actions permitted by applicable law to cause the Investor Designees to be members of the Board (including the appointment of the Investor Designees to the Board).

(d) Subject to clause (e) immediately below, in the event that an Investor Designee ceases to serve on the Board for any reason (including the death, disability or resignation of such person), the Major Investors shall be entitled to appoint a new Investor Designee in the place of such person, and the terms of this Section 7 shall apply equally to such replacement.

(e) In the event that the Applicable Percentage of the Major Investors (and their Affiliates) falls below a threshold set forth in Section 7(b) such that the Major Investors shall lose the right to designate one or more Investor Designees, if one or more Investor Designee has been designated, the Major Investors shall identify which of the Investor Designees shall no longer be an Investor Designee (such person, a "Departing Designee"), and which Investor Designee(s) (if any) will remain as such; for the avoidance of doubt, the terms of this Section 7 shall continue to apply to any Investor Designee who is not a Departing Designee. In the event of a Departing Designee, the Major Investors shall cause the removal or resignation of such Departing Designee prior to the next annual meeting of Iterum shareholders (regardless of whether the term of the class of directors of which he or she is a part expires at such annual meeting), and the provisions of Section 7(b) and (c) shall not apply to such Departing Designee, and in connection therewith (x) Iterum shall not be required to name such Departing Designee on its proxy statement or solicit votes in favor of such Departing Designee and (y) no holder of Ordinary Shares shall be required to cause the Ordinary Shares owned by such shareholder or its Affiliates to be voted in favor of the reelection of such Departing Designee.

(f) The Investor Designees, in addition to all current directors, will be required to: (i) comply with all policies, procedures, processes, codes, rules, standards and guidelines applicable to members of the Board (including with respect to confidentiality); and (ii) complete the Company's standard director and officer questionnaire and other reasonable and customary director onboarding documentation reasonably requested by the Company in connection with the election of Board members and applicable generally to all such Board members.

(g) As a condition to the issuance or sale of any New Securities, Iterum shall cause any recipient of New Securities representing, together with its Affiliates, an Applicable Percentage of 10% or more acquired from Iterum in a private placement to execute a joinder to this Agreement or another instrument satisfactory to the Major Investors, in each case in which such recipient of New Securities agrees to be bound by the terms of this Section 7 and Section 5.5 of the Purchase Agreement. As a condition to the transfer, sale, assignment or other disposition of Ordinary Shares or securities convertible into or exchangeable for Ordinary Shares (including the Exchange Notes) by any Purchaser party to this Agreement other than the Wellington Entities (other than a registered public secondary sale or a bona fide pro rata distribution to the limited partners of such Purchasers), such Purchaser shall cause the transferee to execute a joinder to this Agreement or another instrument satisfactory to the Major Investors and Iterum, in each case in which such transferee agrees to be bound by the terms of this Section 7 and Section 5.5 of the Purchase Agreement. The provisions of this Section 7(g) shall cease to apply (x) with respect to the agreement to be bound by Section 5.5 of the Purchase Agreement, when all approvals described in such Section have been received, and (y) with respect to all other provisions of this Section 7(g), when the Major Investors cease to be entitled to designate Investor Designees in accordance with this Section 7. As a condition to the transfer, sale, assignment or other disposition of RLNs by any Purchaser party to this Agreement other than the Wellington Entities (other than a registered public

secondary sale or a bona fide pro rata distribution to the limited partners of such Purchasers), such Purchaser shall cause the transferee to execute a joinder to this Agreement or another instrument satisfactory to the Major Investors providing the acknowledgments and agreements set forth in Section 9(m) and (n).

(h) Subject to applicable law and listing requirements, the Investor Designees shall be entitled to be a member of any committee of the Board (including an executive or similar committee).

(i) Notwithstanding anything to the contrary in this Agreement, neither the Board nor any committee of the Board shall be under any obligation to nominate or recommend an Investor Designee if, as determined in good faith by the other directors of the Board or any applicable committee thereof based on advice of outside counsel, service by such nominee as a director would reasonably be expected to violate applicable law or the rules or regulations of the primary stock exchange or quotation system on which the Ordinary Shares are listed or quoted. Accordingly, if such requirements are not met and/or such good faith determination is made by the other directors of the Board or applicable committee thereof, the Major Investors shall promptly take all appropriate action to cause any such Investor Designee to resign from the Board, and shall, if required, vote its voting securities in favor of removal of any Investor Designee and any applicable meeting of shareholders.

(j) Any person designated by the Major Investors as an Investor Designee must: (i) qualify as "independent" pursuant to Nasdaq listing standards and satisfy the requirements of all applicable Nasdaq and SEC rules and regulations (including all independence and other criteria required for membership of any committee of the Board on which the Investor Designee is proposed to serve), and (ii) possess the requisite financial and business experience to serve as a director of Iterum (it being understood that each of the executives and investment professionals employed by the Major Investors or their Affiliates shall be deemed to possess such experience). If the Board and all applicable committees of the Board reasonably determine that an Investor Designee satisfies the criteria in the foregoing sentence, the Board shall nominate and appoint such Investor Designee to the Board.

(k) For so long as the Major Investors, collectively, and together with their Affiliates, have the Applicable Percentages set forth in Section 7(b), in the event that any institutional shareholder of Iterum has appointed or designated a person to serve on the board of directors or similar governing body of any Subsidiary of Iterum (a "Subsidiary Board"), the Major Investors shall be entitled to designate a number of Investor Designees to the Subsidiary Board equal to the greater of (x) one Investor Designee or (y) such other number of Investor Designees such that the proportionate representation of Investor Designees on such Subsidiary Board approximates, as closely as possible, the proportionate representation of Investor Designees on the Board.

(l) Commencing upon the delivery of a Designation Notice, each of the Purchasers other than the Wellington Entities covenants and agrees solely with Iterum that such Purchaser shall, cause the voting of all such Ordinary Shares or other outstanding voting equity securities owned (whether beneficially or of record) by them or otherwise available to be voted by them or any of their Affiliates from time to time (whether at any annual or extraordinary general

meeting of the shareholders, by written consent or otherwise), in favor of the election of the Investor Designees to the Board and against any proposal to remove such Investor Designees. Notwithstanding any other provision in this Agreement (but without limiting the obligations of Iterum under this Section 7), if the agreement of any Purchaser to vote or cause to be voted Ordinary Shares or other equity securities in favor of the election of an Investor Designee pursuant to this Section 7 would be deemed to cause the offering of Notes to Purchasers to constitute a change of control in violation of applicable Nasdaq, SEC or other rules, or otherwise violate applicable Nasdaq, SEC or other rules, such agreement shall not be deemed effective until such time as such violation ceases to exist.

8. Confidentiality. Each Purchaser agrees that such Purchaser will keep confidential and will not disclose or divulge any confidential information obtained from the Company pursuant to the terms of this Agreement (including notice of the Company's intention to file a registration statement), unless such confidential information (a) is known or becomes known to the public in general (other than as a result of a breach of this Section 8 by such Purchaser), (b) is or has been independently developed or conceived by such Purchaser without use of the Company's confidential information, or (c) is or has been made known or disclosed to such Purchaser by a third party without a breach of any obligation of confidentiality such third party may have to the Company; provided, however, that a Purchaser may disclose confidential information (i) to its attorneys, accountants, consultants and other professionals to the extent necessary to obtain their services in connection with matters related to the Company; (ii) to any prospective purchaser of any Registrable Securities from such Purchaser, if such prospective purchaser agrees to be bound by the provisions of this Section 8; (iii) to any Affiliate or its or their general or limited partners, members, stockholders, employees, officers or directors, in the ordinary course of business, provided that such Purchaser informs such person that such information is confidential and directs such person to maintain the confidentiality of such information; or (iv) as may otherwise be required by law, regulation, rule, court order, arbitration order or subpoena, provided that such Purchaser promptly notifies the Company of such disclosure and takes reasonable steps to minimize the extent of any such required disclosure. Each Purchaser acknowledges and agrees that the securities laws of the United States and other jurisdictions contain prohibitions on the trading in the securities of Iterum while in possession of material nonpublic information regarding Iterum, and agrees to comply with such restrictions.

9. Miscellaneous.

(a) Amendments and Waivers. This Agreement (other than Sections 6 and 7) may be amended only by a writing signed by the Company, the Guarantors and the Required Purchasers. Other than with respect to Sections 6 and 7, the Company and the Guarantors may take any action herein prohibited, or omit to perform any act herein required to be performed by it, only if the Company and the Guarantors shall have obtained the written consent to such amendment, action or omission to act of the Required Purchasers. Any amendment to Sections 6 or 7, or the defined terms used therein, shall be made by a writing signed by the Company, the Guarantors and the Major Investors; provided that consent of a Purchaser is required in the event that any such amendment would adversely affect the rights of such Purchaser in a material and disproportionate manner relative to the Major Investors or relative to other Purchasers hereunder. The Company and the Guarantors may take any action prohibited by Section 6 or 7, or omit to perform any act required by Section 6 or 7 to be performed by it, only if the Company and the

Guarantors shall have obtained the written consent to such amendment, action or omission to act of the Major Investors.

(b) Notices. All notices and other communications provided for or permitted hereunder shall be made as set forth in Section 6.1 of the Purchase Agreement.

(c) Assignments and Transfers by Purchasers. The provisions of this Agreement shall be binding upon and inure to the benefit of the Purchasers and their respective successors and assigns. A Purchaser may transfer or assign, in whole or from time to time in part, to one or more persons its rights hereunder in connection with the transfer of Registrable Securities by such Purchaser to such person, provided that such Purchaser complies with all laws applicable thereto and the provisions of the Purchase Agreement, the Indenture, the Notes, the RLN Indenture and the RLNs and provides written notice of assignment to the Major Investors, the Company and the Guarantors prior to such assignment being effected, and such transferee agrees in writing and as a condition to the receipt of Registrable Securities to be bound by all of the provisions contained herein.

(d) Assignments and Transfers by the Company. This Agreement may not be assigned by the Company or the Guarantors (whether by operation of law or otherwise) without the prior written consent of the Required Purchasers, which must include the Major Investors for so long as the Major Investors (collectively and together with their Affiliates) own at least 10% of the outstanding Notes and at least 10% of the outstanding RLNs; provided, however, that in the event that the Company or a Guarantor is a party to a merger, consolidation, share exchange or similar business combination transaction in which the Ordinary Shares are converted into the equity securities of another Person, from and after the effective time of such transaction, such Person shall, by virtue of such transaction, be deemed to have assumed the obligations of the Company or such Guarantor, as applicable, hereunder, and the term "Company", "Iterum", "Subsidiary Guarantor(s)" or "Guarantor(s)", as applicable, shall be deemed to refer to such Person and the term "Registrable Securities" shall be deemed to include the securities received by the Purchasers in connection with such transaction unless such securities are otherwise freely tradable by the Purchasers after giving effect to such transaction.

(e) Benefits of the Agreement. The terms and conditions of this Agreement shall inure to the benefit of and be binding upon the respective permitted successors and assigns of the parties. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and assigns any rights, remedies, obligations, or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement.

(f) Counterparts. This Agreement may be executed in several counterparts, and by each Party on separate counterparts, each of which and any photocopies or other electronic transmission (including by PDF) thereof shall be deemed an original, but all of which together shall constitute one and the same agreement.

(g) Titles and Subtitles. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

(h) Severability. Any provision of this Agreement that is prohibited or unenforceable in any jurisdiction shall, as to such jurisdiction, be ineffective to the extent of such prohibition or unenforceability without invalidating the remaining provisions hereof but shall be interpreted as if it were written so as to be enforceable to the maximum extent permitted by applicable law, and any such prohibition or unenforceability in any jurisdiction shall not invalidate or render unenforceable such provision in any other jurisdiction. To the extent permitted by applicable law, the parties hereby waive any provision of law which renders any provisions hereof prohibited or unenforceable in any respect.

(i) Further Assurances. The parties shall execute and deliver all such further instruments and documents and take all such other actions as may reasonably be required to carry out the transactions contemplated hereby and to evidence the fulfillment of the agreements herein contained.

(j) Entire Agreement. This Agreement is intended by the parties as a final expression of their agreement and intended to be a complete and exclusive statement of the agreement and understanding of the parties hereto in respect of the subject matter contained herein. This Agreement supersedes all prior agreements and understandings between the parties with respect to such subject matter.

(k) Specific Performance. Without limiting remedies that may be available at law or in equity, and without limiting Section 2(e)(ii), the parties acknowledge that any failure by any party to comply with their obligations under Section 6 or Section 7 hereof would result in material irreparable injury to the Major Investors for which there is no adequate remedy at law, that it will not be possible to measure damages for such injuries precisely and that, in the event of any such failure, the Major Investors may specifically enforce the parties' obligations under Section 6 or Section 7 without the need to show actual damages and without the need to post a bond or other security.

(l) Governing Law; Consent to Jurisdiction; Waiver of Jury Trial. This Agreement shall be governed by and construed in accordance with the internal laws of the State of New York without regard to the choice of law principles thereof. Each Party agrees that all legal proceedings concerning the interpretations, enforcement and defense of the transactions contemplated by this Agreement (whether brought against a Party hereto or its respective Affiliates, directors, officers, shareholders, employees or agents) shall be commenced exclusively in the state and federal courts sitting in the City of New York. Each Party hereby irrevocably submits to the exclusive jurisdiction of the state and federal courts sitting in the City of New York, borough of Manhattan, for the adjudication of any dispute hereunder or in connection herewith or with any transaction contemplated hereby or discussed herein, and hereby irrevocably waives, and agrees not to assert in any suit, action or other proceeding, any claim that it is not personally subject to the jurisdiction of any such court, that such suit, action or proceeding is improper or is an inconvenient venue for such proceeding. Each Party hereby irrevocably waives personal service of process and consents to process being served in any such suit, action or other proceeding by mailing a copy thereof via registered or certified United States mail or overnight delivery (with evidence of delivery) to such Party at the address in effect for notices to it under this Agreement and agrees that such service shall constitute good and sufficient service of process and notice thereof. Nothing contained herein shall be deemed to limit in any way any right to serve process

in any other manner permitted by law. THE PARTIES HEREBY WAIVE ALL RIGHTS TO A TRIAL BY JURY.

(m) Standstill. Each of the Purchasers covenants and agrees, that in the event that one or more Purchasers are, or are deemed to be, 'acting in concert' (within the meaning of the Irish Takeover Rules), at any time in the future when the aggregate holding of the parties acting in concert exceeds 30% of the share capital of Iterum, no such Purchaser shall acquire shares in Iterum or the Company in circumstances which would trigger a requirement for a mandatory offer under the Irish Takeover Rules and such Purchasers shall enter into a customary standstill agreement with customary terms, conditions and indemnities giving further effect to provisions of this Section 9(m).

(n) Acknowledgement of Holder Representative. Each Purchaser hereby expressly acknowledges and agrees to the appointment of the Holders' Representative, the rights provided thereto, and the obligations of the Purchasers in connection therewith (including the obligations of the Purchasers to indemnify and hold the Holders' Representative harmless) pursuant to RLN Indenture.

[remainder of page intentionally left blank]

IN WITNESS WHEREOF, the parties have executed this Agreement or caused their duly authorized officers to execute this Agreement as of the date first above written.

COMPANY:

ITERUM THERAPEUTICS BERMUDA LIMITED

By: /s/ Louise Barrett
Name: Louise Barrett
Title: Director

ITERUM:

ITERUM THERAPEUTICS PLC

By: /s/ David Kelly
Name: David Kelly
Title: Director

SUBSIDIARY GUARANTOR:

ITERUM THERAPEUTICS INTERNATIONAL LIMITED

By: /s/ Louise Barrett
Name: Louise Barrett
Title: Director

SUBSIDIARY GUARANTOR:

ITERUM THERAPEUTICS US LIMITED

By: /s/ Judith M. Matthews
Name: Judith M. Matthews
Title: Director

SUBSIDIARY GUARANTOR:

ITERUM THERAPEUTICS US HOLDING LIMITED

By: /s/ Judith M. Matthews
Name: Judith M. Matthews
Title: Director

PURCHASERS:

ADVENT LIFE SCIENCES LLP

By: /s/ Kaasim Mahmood
Name: Kaasim Mahmood
Title: Partner

ADVENT LIFE SCIENCES II LP

By: /s/ Kaasim Mahmood
Name: Kaasim Mahmood
Title: Partner

ARIX BIOSCIENCES HOLDINGS LIMITED

By: /s/ Robert Lyne Name: Robert Lyne
Title: Chief Operating Officer & General Counsel

CANAAN X L.P.

By: Canaan Partners X LLC, its general partner

By: /s/ Brent Ahrens
Name: Brent Ahrens
Title: Managing Member

FRAZIER HEALTHCARE VII, L.P.

By: FHM VII, LP, its general partner
By: FHM VII, LLC, its general partner

By: /s/ Patrick Heron Name: Patrick Heron
Title: Manager

FRAZIER HEALTHCARE VII-A, L.P.

By: FHM VII, LP, its general partner
By: FHM VII, LLC, its general partner

By: /s/ Patrick Heron Name: Patrick Heron
Title: Manager

NEW LEAF VENTURES III, L.P.

By: New Leaf Venture Associates III, L.P Its: General Partner
By: New Leaf Venture Management III, L.L.C., Its: General Partner

By: /s/ Craig L. Slutzkin Name: Craig L. Slutzkin
Title: Chief Operating Officer/Chief Financial Officer

NEW LEAF BIOPHARMA OPPORTUNITIES II, L.P.

By: New Leaf BPO Associates II, L.P. Its: General Partner
By: New Leaf BPO Management II, L.L.C. Its: General Partner

By: /s/ Craig L. Slutzkin Name: Craig L. Slutzkin
Title: Chief Operating Officer/Chief Financial Officer

SOFINNOVA VENTURE PARTNERS IX, L.P.

By: Sofinnova Management IX, L.L.C. its General Partner

By: /s/ James I. Healy Name: James I. Healy
Title: Managing Member

DOMAIN PARTNERS IX, L.P.

By: One Palmer Square Associates IX, L.L.C.

By: /s/ Lisa A. Kraeutler
Name: Lisa A. Kraeutler
Title: Attorney-in-fact

PIVOTAL BIOVENTURE PARTNERS FUND, LP

By: Pivotal bioVenture Partners Fund I GP, LP
By: Pivotal bioVenture Partners Fund I GP U.G.P., Ltd.

By: /s/ Robert Hopfner Name: Robert Hopfner
Title: Managing Partner

SARISSA CAPITAL OFFSHORE MASTER FUND LP

By: /s/ Patrice Bonfiglio Name: Patrice Bonfiglio
Title: Chief Financial Officer

SARISSA CAPITAL CATAPULT FUND LLC

By: /s/ Patrice Bonfiglio Name: Patrice Bonfiglio
Title: Chief Financial Officer

SARISSA CAPITAL HAWKEYE FUND LP

By: /s/ Patrice Bonfiglio Name: Patrice Bonfiglio
Title: Chief Financial Officer

2B LLC

By: SilverArc Capital Management, LLC acting as Investment manager

By: /s/ Andrew Timpson Name: Andrew Timpson
Title: Chief Operating Officer

683 CAPITAL PARTNERS, LP

By: /s/ Joseph Patt Name: Joseph Patt
Title: Member of the General Partner

BLACKWELL PARTNERS LLC – SERIES A

By: /s/ Justin B. Nixon Name: Justin B. Nixon
Title: Investment Manager DUMAC, Inc.,
Authorized Signatory

By: /s/ Jannine M. Lall Name: Jannine M. Lall
Title: Investment Manager DUMAC, Inc.,
Authorized Signatory

CVI INVESTMENTS, INC

By: Heights Capital Management, Inc., its authorized signatory

By: /s/ Martin Kobinger Name: Martin Kobinger
Title: Investment Manager

EMPERY MASTER ONSHORE, LLC

By: Empery Asset Management LP, its authorized agent

By: /s/ Brett Director Name: Brett Director
Title: General Counsel

EMPERY TAX EFFICIENT, LP

By: Empery Asset Management LP, its authorized agent

By: /s/ Brett Director Name: Brett Director
Title: General Counsel

EMPERY TAX EFFICIENT II, LP

By: Empery Asset Management LP, its authorized agent

By: /s/ Brett Director Name: Brett Director
Title: General Counsel

NORTH SOUND TRADING, LP

By: /s/ Brian Miller Name: Brian Miller
Title: President of the General Partner

RA CAPITAL HEALTHCARE FUND, L.P.

By: RA Capital Healthcare Fund GP, LLC Its General Partner

By: /s/ Peter Kolchinsky Name: Peter Kolchinsky
Title: Manager

LINCOLN PARK CAPITAL FUND, LLC

By: Lincoln Park Capital, LLC By: Rockledge Capital Corporation

By: /s/ Joshua Scheinfeld Name: Joshua Scheinfeld
Title: President

S.H.N. FINANCIAL INVESTMENTS LTD

By: /s/ Nir Shamir Name: Nir Shamir
Title: Owner

SABBY VOLATILITY WARRANT MASTER FUND, LTD

By: /s/ Robert Grundstein Name: Robert Grundstein
Title: COO of Investment Manager

SILVERARC CAPITAL ALPHA FUND I, L.P.

By: SilverArc Capital Management, LLC acting as Investment manager

By: /s/ Andrew Timpson Name: Andrew Timpson
Title: Chief Operating Officer

SILVERARC CAPITAL ALPHA FUND II, L.P.

By: SilverArc Capital Management, LLC acting as Investment manager

By: /s/ Andrew Timpson Name: Andrew Timpson
Title: Chief Operating Officer

GARY D. COHN

By: /s/ Gary D. Cohn Name: Gary D. Cohn

SALTHILL PARTNERS, L.P.

By: Wellington Management Company LLP, as investment adviser

By: /s/ Emily Babalas Name: Emily Babalas
Title: Managing Director & Counsel

SALTHILL INVESTORS (BERMUDA) L.P.

By: Wellington Management Company LLP, as investment adviser

By: /s/ Emily Babalas Name: Emily Babalas
Title: Managing Director & Counsel

EXHIBIT A

Plan of Distribution

The selling securityholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling ordinary shares [, notes or RLNs] (which we refer to [collectively] as the "securities") or interests in the securities received after the date of this prospectus from a selling securityholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their securities or interests in the securities on any stock exchange, market or trading facility on which the securities are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices. The selling securityholders will act independently of us in making decisions with respect to the timing, manner and size of each sale.

The selling securityholders may sell the securities by any one or more of the following methods:

– ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

– block trades in which the broker-dealer so engaged will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;

– purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

– an exchange distribution in accordance with the rules of the applicable exchange;

– privately negotiated transactions;

– short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;

– through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;

– broker-dealers may agree with the selling securityholders to sell a specified number of such securities at a stipulated price per security;

– a combination of any such methods of sale; and

– any other method permitted by applicable law.

The selling securityholders may, from time to time, pledge or grant a security interest in some or all of the securities owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the securities, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933, as amended (the "Securities Act"), amending

the list of selling securityholders to include the pledgee, transferee or other successors in interest as selling securityholders under this prospectus. The selling securityholders also may transfer the securities in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of the securities or interests therein, the selling securityholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the securities in the course of hedging the positions they assume. The selling securityholders may also sell the securities short and deliver these securities to close out their short positions, or loan or pledge the securities to broker-dealers that in turn may sell these securities. The selling securityholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of the securities offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling securityholders from the sale of the securities offered by them will be the purchase price of the securities less discounts or commissions, if any. Each of the selling securityholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of the securities to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling securityholders also may resell all or a portion of the securities in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The selling securityholders and any underwriters, broker-dealers or agents that participate in the sale of the securities or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the securities may be underwriting discounts and commissions under the Securities Act. Selling securityholders who are “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

In offering the securities covered by this prospectus, the selling securityholders and any broker-dealers who execute sales for the selling securityholders may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. Any profits realized by the selling securityholders and the compensation of any broker-dealer may be deemed to be underwriting discounts and commissions.

To the extent required, the securities to be sold, the names of the selling securityholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the securities may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition,

in some states the securities may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling securityholders that the anti-manipulation rules of Regulation M promulgated under the Securities Exchange Act of 1934, as amended, may apply to sales of shares in the market and to the activities of the selling securityholders and their affiliates. In addition, to the extent applicable we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling securityholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling securityholders may indemnify any broker-dealer that participates in transactions involving the sale of the securities against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling securityholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the securities offered by this prospectus. We have agreed with the selling securityholders to keep the registration statement of which this prospectus constitutes a part (or any replacement registration statement and related prospectus) effective until the earlier of (1) such time as all of the securities covered by this prospectus or replacement prospectus, as applicable, have been sold, (2) the date on which all of the securities covered by this prospectus or replacement prospectus, as applicable, may be sold without restriction pursuant to Rule 144 of the Securities Act and without the requirement to be in compliance with Rule 144(c)(1) (or any successor thereto) of the Securities Act and (3) the date that is six years following the date the initial registration statement filed pursuant to the investor rights agreement between us and the selling securityholders initially becomes effective.

* * * * *

Exhibit 21.1

LIST OF SUBSIDIARIES OF ITERUM THERAPEUTICS PLC

Subsidiary	Jurisdiction
Iterum Therapeutics International Limited	Ireland
Iterum Therapeutics US Limited	Delaware
Iterum Therapeutics US Holding Limited	Delaware
Iterum Therapeutics Bermuda Limited	Bermuda

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Shareholders and Board of Directors
Iterum Therapeutics plc:

We consent to the incorporation by reference in the registration statement (No. 333-225236 and 333-230496) on Forms S-8 and the registration statement (No. 333-232569) on Form S-3 of Iterum Therapeutics plc of our report dated March 12, 2020, with respect to the consolidated balance sheets of Iterum Therapeutics plc as of December 31, 2019 and 2018, the related consolidated statements of income, comprehensive income, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2019, and the related notes, which report appears in the December 31, 2019 annual report on Form 10-K of Iterum Therapeutics plc.

Our report dated March 12, 2020 contains an explanatory paragraph that states that the Company has suffered recurring losses from operations and has a net capital deficiency, which raise substantial doubt about its ability to continue as a going concern. The consolidated financial statements do not include any adjustments that might result from the outcome of that uncertainty. Also, our report on the consolidated financial statements refers to a change to the method of accounting for leases as of January 1, 2019 due to the adoption of ASC Topic 842, Leases.

/s/ KPMG

Dublin, Ireland
March 12, 2020

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Corey Fishman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Iterum Therapeutics plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2020

By: /s/ Corey Fishman

Corey Fishman
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Judith Matthews, certify that:

1. I have reviewed this Annual Report on Form 10-K of Iterum Therapeutics plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2020

By: /s/ Judith Matthews

Judith Matthews
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Iterum Therapeutics plc (the "Company") for the year ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Corey Fishman, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to his knowledge on the date hereof:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 12, 2020

By: /s/ Corey Fishman

Corey Fishman
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Iterum Therapeutics plc (the "Company") for the year ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Judith Mathews, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to her knowledge on the date hereof:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 12, 2020

By: /s/ Judith Matthews

Judith Matthews
Chief Financial Officer
(Principal Financial and Accounting Officer)