Table of Contents

As filed with the U.S. Securities and Exchange Commission on May 16, 2018

Registration No. 333-224582

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 2
to
FORM S-1
REGISTRATION STATEMENT

UNDER
THE SECURITIES ACT OF 1933

Iterum Therapeutics plc

(Exact Name of Registrant as Specified in Its Charter)

Ireland	2834	98-1283148
(State or other Jurisdiction of Incorporation or Organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a 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 ☒ (Do not check if a smaller reporting company)	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 to Section 7(a)(2)(B) of the Securities Act. ☒

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)

Ordinary shares, $0.01 par value per share	$98,133,312	$12,218

(1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(o) under the Securities Act. Includes the offering price of shares that the underwriters have the over-allotment option to purchase.
(2) The registrant previously paid $11,454 in connection with a prior filing of this Registration Statement on May 1, 2018.

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MAY 16, 2018

PROSPECTUS

5,333,333 Ordinary Shares

This is our initial public offering. We are offering 5,333,333 of our ordinary shares.

Prior to this offering, there has been no public market for our ordinary shares. We expect the initial public offering price to be between $14.00 and $16.00 per share. We have applied to list our ordinary shares on the Nasdaq Global Market under the symbol "ITRM."

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. See "Prospectus Summary—Emerging Growth Company Status."

You should consider the risks we have described in " Risk Factors" beginning on page 10.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Initial public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds, before expenses, to us	$	$

(1) We refer you to "Underwriting" beginning on page 173 of this prospectus for additional information regarding underwriting compensation.

Certain of our directors and existing shareholders, or their affiliates, have indicated an interest in purchasing up to an aggregate of approximately $35.0 million of our ordinary shares in this offering. These shares will be offered and sold on the same terms as the other shares that are being offered and sold in this offering to the public. Although we anticipate that these parties will purchase all of the ordinary shares that these parties have indicated an interest in purchasing, indications of interest are not binding agreements or commitments to purchase and any of these parties may determine to purchase more, less or no shares in this offering.

We have granted the underwriters an over-allotment option to purchase up to an additional 799,999 ordinary shares on the same terms and conditions.

The underwriters expect to deliver the ordinary shares on or about , 2018.

Leerink Partners **RBC Capital Markets**

Guggenheim Securities

Needham & Company

The date of this prospectus is , 2018.

TABLE OF CONTENTS

	Page
Prospectus Summary	1
Risk Factors	10
Special Note Regarding Forward-Looking Statements and Industry Data	64
Use of Proceeds	66
Dividend Policy	67
Capitalization	68
Dilution	70
Selected Consolidated Financial Data	72
Management's Discussion and Analysis of Financial Condition and Results of Operations	74
Business	89
Management	124
Executive Compensation	133
Certain Relationships and Related Party Transactions	140
Principal Shareholders	142
Description of Share Capital	145
Shares Eligible for Future Sale	162
Taxation	165
Underwriting	173
Legal Matters	181
Experts	181
Where You Can Find Additional Information	181
Index to Financial Statements	F-1

We are responsible for the information contained in this prospectus and in any free writing prospectus we prepare and authorize. Neither we nor any of the underwriters have authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. Neither we nor the underwriters are making an offer to sell these securities in any jurisdiction where such offer and sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the cover of this prospectus. Our business, financial condition, results of operations, and future growth prospects may have changed since that date.

Persons who come into possession of this prospectus and any applicable free writing prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus and any such free writing prospectus applicable to that jurisdiction.

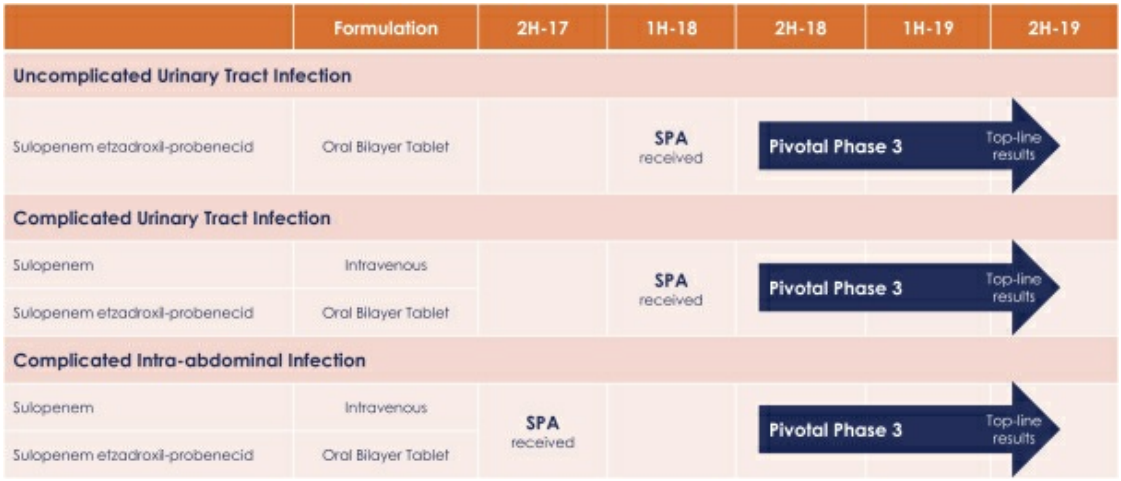
PROSPECTUS SUMMARY

This summary highlights information contained in other parts of this prospectus. Because it is only a summary, it does not contain all of the information that you should consider before investing in our ordinary shares and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus. You should read the entire prospectus carefully, especially "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes, before deciding to buy our ordinary shares. Unless the context requires otherwise, references in this prospectus to "Iterum," the "company," "we," "us," and "our" refer to Iterum Therapeutics plc and its wholly owned subsidiaries.

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, which we licensed from Pfizer Inc. (Pfizer) in November 2015, 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. Pfizer also developed an oral prodrug, sulopenem etzadroxil, which we further enhanced with the addition of probenecid and combined into a single bilayer tablet, which we refer to as oral sulopenem. Both oral sulopenem and sulopenem 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 believe there are 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.

We plan to initiate a Phase 3 clinical program in the second half of 2018 for the treatment of adults in three indications: uUTI, complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (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 intend to conduct the Phase 3 clinical trials under Special Protocol Assessment (SPA) agreements from the FDA. We expect to complete enrollment and produce top-line data for all three clinical trials in the second half of 2019, and to submit our new drug applications (NDAs) to the FDA by the end of 2019.



The Medical Need

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

Based on market research, physicians estimated that approximately 35% of uUTI patients are at elevated risk for treatment failure. Proper antibiotic treatment of 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, those 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. 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. 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 fluoroquinolone antibiotics directing healthcare professionals to reserve fluoroquinolones for patients with no other treatment alternatives. The combination of growing prevalence of bacterial resistance and FDA-mandated safety label changes for fluoroquinolones have left physicians in search of new oral treatment alternatives to safely and effectively treat their uUTI patients.

Our Solution: Sulopenem Program

Our sulopenem program has the potential to offer a solution to the problem of antibiotic resistance and the toxicity 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. 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. 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. Adverse event data from these trials 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. We have further enhanced this prodrug formulation with the addition of probenecid to extend sulopenem's half-life and enhance its antibacterial potential.

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.

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.

Sulopenem etzadroxil has an issued composition of matter patent in the United States (which we have exclusively licensed from Pfizer) that is scheduled to expire in 2029, subject to potential extension to 2034 under the Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Act). In addition, the FDA has designated sulopenem and oral sulopenem as Qualified Infectious Disease Products (QIDP) for the indications of uUTI, cUTI and cIAI pursuant to the Generating Antibiotic Incentives Now Act (the GAIN Act), which provides the potential for a more rapid NDA review cycle and which could add five years to any regulatory exclusivity period that we may be granted. None of our licensed patents cover the IV formulation of sulopenem.

Our Commercialization Plan

If the FDA approves oral sulopenem and sulopenem, we plan to build a targeted commercial infrastructure to launch both product candidates in the United States. Data from a study we commissioned in 2017 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 plan to employ a dual sourcing strategy for critical elements of our sulopenem supply chain. 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 by the end of 2019. We plan to utilize a third-party facility to manufacture sulopenem tablets and another third party to manufacture the IV vials. Potential additional sources to manufacture sulopenem tablets and IV vials have also been identified.

Our Management Team and Investors

We were founded in June 2015 by former executives of Durata Therapeutics, Inc. (Durata), a biopharmaceutical company, which developed dalbavancin, another antibiotic from the Pfizer portfolio, and successfully obtained FDA approval, launched the product in the United States and submitted a marketing authorization application (MAA) to the EMA (approval was received in 2015). Durata was acquired by Allergan plc (Allergan, formerly Actavis, Inc.) in late 2014. To date, we have raised approximately $120 million to develop our sulopenem program from a leading investor group including Advent Life Sciences LLP, Arix Bioscience plc, Bay City Capital LLC, Canaan Partners, Domain Associates, L.L.C., Frazier Healthcare Partners, New Leaf Venture Partners, Pivotal bioVenture Partners and Sofinnova Ventures, Inc., as well as our founders. Pfizer is also one of our shareholders.

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;
- obtain regulatory approval for oral sulopenem and sulopenem in the United States and subsequently in the European Union;

- maximize commercial potential of our sulopenem program;
- pursue the development of oral sulopenem and sulopenem in additional indications; and
- build a portfolio of differentiated anti-infective products.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our ordinary shares. These risks are discussed more fully in the section titled "Risk Factors" and include, among others:

- 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 will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of our sulopenem program.
- 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 or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately may be unable to complete, the development and commercialization of oral sulopenem, sulopenem or any other product candidate.
- We face substantial competition from other pharmaceutical and biotechnology companies and our business may suffer if we fail to compete effectively.
- If we fail to comply with our obligations in our agreement with Pfizer, we could lose valuable intellectual property rights that are necessary to our development and commercialization of oral sulopenem and sulopenem.
- 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.
- 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.
- Our product candidates 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.
- Delays or issues with the manufacture of preclinical, clinical or commercial supplies of oral sulopenem and sulopenem could negatively impact our development and commercialization plans.

Emerging Growth Company Status

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act (the JOBS Act), enacted in April 2012; therefore, we intend to take advantage of certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by an independent registered public accounting firm pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, 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 not previously approved. We may take advantage of these exemptions for up to five years or until we are no longer an "emerging growth company," whichever occurs earlier.

The JOBS Act permits an emerging growth company to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

Corporate Information

We were incorporated in Ireland in June 2015 and were re-registered as a public limited company in March 2018 under the name Iterum Therapeutics plc. 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. Our U.S. headquarters are located at 200 South Wacker Dr., Suite 650, Chicago, IL 60606, and our telephone number is (312) 778-6070. Our corporate website address is www.iterumtx.com. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

Iterum, our logo and our other registered or common law trademarks, trade names or service marks appearing in this prospectus are owned by us. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

The Offering

Ordinary shares offered by us	5,333,333 shares
Ordinary shares to be outstanding after this offering	13,142,756 shares
Over-allotment option to purchase additional shares	We have granted the underwriters a 30-day over-allotment option to purchase up to an additional 799,999 ordinary shares.
Use of proceeds	We estimate that the net proceeds to us from this offering will be approximately $71.4 million, or approximately $82.6 million if the underwriters exercise their over-allotment option in full, based on an assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering, together with our cash, cash equivalents, short-term investments and available borrowing under our credit facility, to fund our Phase 3 clinical trials of oral sulopenem and sulopenem, for payments to Pfizer pursuant to the exclusive license agreement we have entered into with Pfizer, and for working capital and other general corporate purposes, including regulatory, manufacturing, clinical supply and related costs. See "Use of Proceeds" for additional information.
Proposed Nasdaq Global Market symbol	"ITRM"
Risk Factors	You should carefully read the section titled "Risk Factors" and other information included in this prospectus for a discussion of factors that you should consider before deciding to invest in our ordinary shares.

The number of ordinary shares to be outstanding after this offering is based on 7,809,423 ordinary shares outstanding as of March 31, 2018 and excludes:

- 248,128 ordinary shares issuable upon the exercise of outstanding stock options as of March 31, 2018, with a weighted-average exercise price of $3.31 per share;
- 194,901 ordinary shares reserved for future issuance under our 2015 Equity Incentive Plan as of March 31, 2018; all shares reserved for future issuance and not subject to an outstanding stock option will cease to be available for issuance at the time our 2018 Equity Incentive Plan becomes effective in connection with this offering;
- 1,018,459 ordinary shares reserved for future issuance under our 2018 Equity Incentive Plan, as well as any increases in the number of ordinary shares reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement for this offering. Of the 1,018,459 ordinary shares reserved for future issuance under our 2018 Equity Incentive Plan, upon the execution of the underwriting agreement for this offering, options to purchase 417,867 ordinary shares will be granted to our employees and additional options and/or restricted stock units will be granted to our non-employee directors; and

- 19,890 ordinary shares issuable upon exercise of outstanding warrants issued subsequent to March 31, 2018 at a price of $18.85 per share.

In addition, unless we specifically state otherwise, all information in this prospectus assumes:

- the filing and effectiveness of our amended and restated constitution in connection with the closing of this offering;
- the conversion of all outstanding preferred shares into an aggregate of 7,396,313 ordinary shares immediately prior to the closing of this offering and the cancellation of the series preferred share classes;
- a one for 15.71 reverse stock split, and a renominalization of the par value of our ordinary shares, effective as of May 15, 2018;
- no exercise of outstanding stock options;
- no exercise by the underwriters of their over-allotment option to purchase up to an additional ordinary shares from us; and
- the conversion of outstanding warrants exercisable for 19,890 Series B-2 preferred shares into warrants exercisable for 19,890 ordinary shares immediately prior to the closing of this offering.

Certain of our directors and existing shareholders, or their affiliates, have indicated an interest in purchasing up to an aggregate of approximately $35.0 million of our ordinary shares in this offering. These shares will be offered and sold on the same terms as the other shares that are being offered and sold in this offering to the public. Although we anticipate that these parties will purchase all of the ordinary shares that these parties have indicated an interest in purchasing, indications of interest are not binding agreements or commitments to purchase and any of these parties may determine to purchase more, less or no shares in this offering.

Summary Financial Data

The following tables summarize our consolidated financial and other data. The consolidated statements of operations data for the years ended December 31, 2016 and 2017 and the consolidated balance sheet data as of December 31, 2017 are derived from our audited consolidated financial statements included elsewhere in this prospectus. The consolidated statements of operations data for the three months ended March 31, 2017 and 2018 and the consolidated balance sheet data as of March 31, 2018 are derived from our unaudited interim consolidated financial statements included elsewhere in this prospectus. Our unaudited interim consolidated financial statements were prepared on a basis consistent with our audited consolidated financial statements and include, in our opinion, all adjustments, consisting only of normal recurring adjustments, that we consider necessary for a fair presentation of the financial information set forth in those statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in any future period, and the results for the three months ended March 31, 2018 are not necessarily indicative of the results to be expected for the full year or any other period.

You should read this data together with our consolidated financial statements and related notes included elsewhere in this prospectus and the sections titled "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	Year Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
			(unaudited)	
	(in thousands, except share and per share data)			
Consolidated Statements of Operations Data:				
Revenue	$ —	$ 508	$ —	$ 191
Operating expenses:				
Research and development	(10,101)	(25,499)	(4,534)	(10,879)
General and administrative	(3,258)	(4,464)	(1,008)	(1,515)
Total operating expenses	(13,359)	(29,963)	(5,542)	(12,394)
Operating loss	(13,359)	(29,455)	(5,542)	(12,203)
Interest income, net	—	277	—	85
Other income/(expense), net	8	216	(68)	61
Total other income	8	493	(68)	146
Loss before income taxes	(13,351)	(28,962)	(5,610)	(12,057)
Income tax expense	(113)	(444)	(227)	(89)
Net loss and comprehensive loss	$(13,464)	$ (29,406)	$ (5,837)	$ (12,146)
Net loss attributable to ordinary shareholders	$(13,464)	$ (29,406)	$ (5,837)	$ (12,146)
Net loss per share attributable to ordinary shareholders, basic and diluted[1]	$(568.87)	$ (170.84)	$(103.68)	$ (61.36)
Weighted average ordinary shares outstanding, basic and diluted	23,668	172,130	56,301	197,949
Pro forma net loss per share attributable to ordinary shareholders, basic and diluted (unaudited)		$ (5.02)		$ (1.60)
Pro forma weighted average ordinary shares outstanding, basic and diluted (unaudited)		5,858,793		7,594,262

(1) Net loss per share, basic and diluted, is the same due to our net loss.

	As of March 31, 2018		
	Actual	Pro Forma(1)	Pro Forma As Adjusted(2)(3)
	(in thousands)		
Consolidated Balance Sheet Data:			
Cash, cash equivalents, restricted cash and short-term investments	$59,754	$ 74,754	$ 146,154
Working capital(4)	57,062	72,062	143,462
Total assets	68,131	83,131	154,531
Credit facility	—	15,000	15,000
Total liabilities	8,401	23,401	23,401
Convertible preferred shares	74	—	—
Total shareholders' equity	59,656	59,730	131,130

(1) The pro forma column reflects (a) the conversion of all outstanding preferred shares into 7,396,313 of our ordinary shares immediately prior to the closing of this offering, (b) the drawdown of $15.0 million under our credit facility with Silicon Valley Bank in April 2018, and (c) the filing and effectiveness of our amended and restated constitution upon the closing of this offering.

(2) The pro forma as adjusted column reflects the sale of 5,333,333 ordinary shares in this offering at an assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(3) Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) each of cash, cash equivalents and short-term investments, working capital, total assets, and total shareholders' equity on a pro forma as adjusted basis by $5.0 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus remains the same, after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us. Similarly, each increase (decrease) by 1,000,000 shares in the number of shares offered by us would increase (decrease) each of cash, cash equivalents and short-term investments, working capital, total assets, and total shareholders' equity on a pro forma as adjusted basis by $14.0 million, assuming that the assumed initial public offering price remains the same, after deducting the estimated underwriting discounts and commissions. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

(4) Working capital is equal to current assets minus current liabilities.

RISK FACTORS

Investing in our ordinary shares involves a high degree of risk. You should carefully consider the risks described below, together with the other information contained in this prospectus, including our consolidated financial statements and the related notes appearing at the end of this prospectus, before making your decision to invest in our ordinary shares. We cannot assure you that any of the events discussed in the risk factors below will not occur. These risks could have a material and adverse impact on our business, results of operations, financial condition and cash flows, and if so our future prospects would likely be materially and adversely affected. If any of such events were to happen, the trading price of our ordinary shares could decline, and you could 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 March 31, 2018, we had an accumulated deficit of $66.9 million. Our product candidates, oral sulopenem and sulopenem (together, the sulopenem program), are in clinical development, have not been approved for sale and we may never have our product candidates approved for commercialization. We have financed our operations through private placements of our preferred shares. 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 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, which we expect will occur in 2018 and 2019, and our three planned pivotal Phase 3 clinical trials which we plan to initiate in the second half of 2018;
- 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);
- 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 transition to a public reporting company; and
- acquire or in-license other product candidates or technologies.

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:

- commencing, enrolling and successfully completing Phase 3 clinical trials of our sulopenem program in our three initial 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; 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 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.

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 you to lose all or part of your investment.

We will require additional capital to fund our operations, and if we fail to obtain necessary financing, 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 commence and advance our 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. 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. Accordingly, 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. 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.

We believe that the net proceeds from this offering, together with our existing cash, cash equivalents, short-term investments, and available borrowings under our credit facility, will enable us to fund our operating expenses and capital expenditure requirements through the fourth quarter of 2019. Our cash forecasts are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. 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 planned clinical trials of oral sulopenem and sulopenem;
- 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 (the Pfizer License) or other future license agreements;
- 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.

Upon completion of this offering, our non-dilutive source of funding is expected to be a sub-award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) program (the CARB-X Award). The CARB-X Award supports preclinical and clinical trials in support of our potential regulatory filings for oral sulopenem and sulopenem, along with chemistry, manufacturing and controls optimization and development of our commercial bilayer tablet. The CARB-X Award is structured as a cost reimbursement arrangement. In June 2017, CARB-X awarded funds of up to $1.5 million to advance the development of our sulopenem program and during the year ended December 31, 2017 and the three months ended March 31, 2018, we recognized $0.5 million and $0.2 million of revenue, respectively, under this award. The CARB-X Award is subject to termination by the Trustees of Boston University with 30 days, written notice, and to the availability of federal government and non-government funding.

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 with Silicon Valley Bank (SVB) pursuant to which SVB agreed to lend the Borrowers up to $30 million in two term loans. $15 million of the secured credit facility was available on closing and the other $15 million is available at our option upon the satisfaction of certain draw requirements. In connection with the initial drawdown, we issued warrants to SVB and Life Sciences Fund II LLC (LSF) to purchase an aggregate of 19,890 Series B-2 preferred shares. If we draw down the second term loan, each of SVB and LSF will be entitled, pursuant to additional share warrants issued to each of them at closing, to purchase such number of additional ordinary shares in an aggregate amount equal to 2.5% of the funded amount, 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. 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.

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 the development team have successfully developed and registered other antibiotics, as Iterum we have limited experience and have 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. 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, including purchasers of ordinary shares in this offering, 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, we may 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.

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, your ownership interest may be materially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as an ordinary shareholder. In addition, if we make an additional draw under our secured credit facility, we will be required to issue additional warrants. 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 intend to focus on developing our sulopenem program for the specific indications of uUTI, cUTI and cIAI, all of which are focused on 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.

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.

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 our three planned pivotal Phase 3 clinical trials of oral sulopenem and sulopenem, which we plan to initiate in the second half of 2018;
- 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 Inc. (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 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.

As Iterum, we have no experience in obtaining regulatory approval for a drug.

As Iterum, we have 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 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, nonclinical 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 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 nonclinical studies or clinical trials. The results of preclinical and other nonclinical studies and/or early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Notwithstanding any promising results in early nonclinical 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, while EMA guidelines recommend microbiologic outcome. 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.

The clinical development of oral sulopenem, sulopenem and other product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to achieve 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. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

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 you that any Phase 3 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 expect to conduct 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 prospective contract research organizations (CROs), and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and 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 noncompliance 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 you that our clinical trials will begin as planned or 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. We may not be able to initiate, continue or complete 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.

The inclusion and exclusion criteria for our contemplated Phase 3 clinical trials of oral sulopenem and sulopenem may adversely affect our enrollment rates for patients in these clinical trials. 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 CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and we will 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 you that any of our current clinical trials, planned Phase 3 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 planned pivotal 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 conducted Phase 3 clinical trials of oral sulopenem or sulopenem in the indications uUTI, cUTI and cIAI, and we have not documented to the satisfaction of regulators that these treatments are effective in treating uUTIs, cUTIs or cIAIs in humans. Although we believe that oral sulopenem and sulopenem have the potential to treat uUTIs, cUTIs, and cIAIs 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 planned clinical trials, and we cannot guarantee that oral sulopenem will demonstrate the expected efficacy in our planned pivotal Phase 3 clinical trial patients. We also cannot guarantee that the projections made from the pharmacokinetic and pharmacodynamic models that we developed from nonclinical and clinical oral sulopenem and sulopenem studies will be validated in our planned pivotal Phase 3 clinical trials.

Other companies in the pharmaceutical industry have frequently suffered significant setbacks in later clinical trials, even after achieving promising results in earlier nonclinical 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. There may be unforeseen serious adverse

events or side effects that differ from those seen 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 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 planned 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 prevented 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 our 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;
- 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 risk evaluation and mitigation strategy;
- 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 and patients, 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 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 in the United States 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. 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 on our own 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.

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 currently evaluating our commercialization strategy outside the United States. For those countries in which we choose not to commercialize directly ourselves, 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 our 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 ceftibuten clavulanate from Achaogen, Inc., tebipenem pivoxil from Spero Therapeutics, Inc., delafloxacin from Melinta Therapeutics, Inc. and omadacycline from Paratek Pharmaceuticals, 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 Inc., Vabomere from Melinta Therapeutics, Inc., and Zerbaxa from Merck & Co. There are also a number of IV-administered product candidates in late-stage clinical development that are intended to treat resistant gram-negative infections, including plazomicin from Achaogen, Inc., cefiderocol from Shionogi & Co. Ltd. and imipenem-relabactam from Merck & Co.

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 and management 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 and cIAI. 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.

We currently expect that oral sulopenem will be used in the community setting. The commercial success of oral sulopenem will depend substantially, both in the United States and outside the United States, on the extent to which adequate coverage and reimbursement for this 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 of 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.

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 million, our insurance may be insufficient to reimburse us for any expenses or losses we may suffer, and we will be required to increase our product liability insurance coverage for our advanced clinical trials that we plan to initiate. 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 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 noncompliance. 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, customers 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 Irish, 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 loss of reputation, 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 patents and know-how related to sulopenem etzadroxil and certain know-how related to the IV formulation of sulopenem. The Pfizer License imposes, and we may enter into additional agreements, including license agreements, with other parties in the future that impose diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us.

The Pfizer License gives us exclusive worldwide rights to develop, manufacture, and commercialize sulopenem etzadroxil and sulopenem, or any other prodrug of sulopenum 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 nonrefundable upfront fee of $5.0 million and are obligated to pay Pfizer milestone payments upon the achievement of specified clinical, 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 as additional payment for the licensed rights. For a more detailed summary of the Pfizer License, please see the section titled “Business—Pfizer License Agreement.”

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 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. 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.

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 nonclinical 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 contract research organizations (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 nonclinical studies and clinical trials, we remain responsible for ensuring that each of our nonclinical 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 you 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 other 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 the agreement between 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. 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 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 current Good Manufacturing Practing, or 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 nonclinical 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 planned 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 or patent applications 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 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 conditions, 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 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. The patent applications that we may own in the future or in-license may fail to result in issued patents with claims that cover our current and future product candidates in the United States or in other countries. Patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, a patent issues from such applications, and then only to the extent the issued claims cover the technology.

If any patent applications we may 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 conditions, 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 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 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. For example, under the CARB-X grant funding program, the U.S. Department of Health and Human Services (HHS) awarded us a grant in connection with research to reduce the threat to human health from antimicrobial resistance and we granted the U.S. government a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the U.S. government any inventions arising out of our research globally. In addition, under such agreement, if we or our licensees do not use commercially reasonable efforts to exploit or further the development of any intellectual property rights we have generated out of such research within five years of the end date of our research project, Wellcome Trust Limited has the option to take responsibility for the commercialization and exploitation of such intellectual property rights, including by way of sale, assignment and license of such intellectual property rights.

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 (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 and cIAI, however that does not guarantee that we will receive any regulatory exclusivity extensions or that any such extensions 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 Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union. The Hatch-Waxman Amendments permit 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, such as Europe, 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 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 any future pending patent applications will not lead to issued patents;
- 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;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

The USPTO has developed in the last few years regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA, and, 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. 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 offices 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 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 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 noncompliance 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 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 conditions, results of operations and 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 a pending application for the trademark "Iterum" in Canada, and we have registered trademarks for "Iterum" in the United States, European Union, Japan and Switzerland. 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 have also not yet registered trademarks for any of our product candidates in any jurisdiction. Any trademark applications we may file for our product candidates 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 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, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects 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.

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 conditions, results of operations and 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 for sulopenem and oral sulopenem for the indications of uUTI, cUTI and cIAI 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 nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe that the nonclinical 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 expect to conduct our Phase 3 clinical trials pursuant to SPA agreements, the FDA may still require us to conduct additional nonclinical 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 are insufficient for approval and require additional nonclinical, 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 bodies can delay, limit or deny approval of our product candidates or require us to conduct additional nonclinical or clinical testing or abandon a program for many reasons, including:

- although we expect to conduct our Phase 3 clinical trials pursuant to SPA agreements, the FDA or the applicable foreign regulatory agency's disagreement with the design or implementation of our clinical trials;
- 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;
- the FDA's or the applicable foreign regulatory agency's disagreement with the interpretation of data from nonclinical 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 nonclinical 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 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 outside the United States, but believe that 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. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union 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 nonclinical 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 nonclinical 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 nonclinical 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 post-marketing 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 labeling 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 on-going;
- 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 noncompliance;
- 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 involve 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 HHS 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; 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.

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.

Certain countries in which we operate have, or are developing, laws protecting the confidentiality of certain patient health information. EU member states and other jurisdictions have adopted data protection laws and regulations, which impose significant compliance obligations.

For example, the EU Data Protection Directive, as implemented into national laws by the EU member states, imposes strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. Data protection authorities from different EU member states may interpret the EU Data Protection Directive and national laws differently, which adds to the complexity of processing personal data in the EU, and guidance on implementation and compliance practices are often updated or otherwise revised. The EU Data Protection Directive prohibits the transfer of personal data to countries outside of the EU member states that are not considered by the European Commission to provide an adequate level of data protection, and transfers of personal data to such countries can only be made in certain circumstances—for example, where the transfer is required by law or the data subject (i.e. the individual to

whom the personal data relates) has given his or her consent to the transfer. We have policies and practices that we believe make us compliant with applicable privacy regulations. Nevertheless, any failure to comply with the rules arising from the EU Data Protection Directive and related national laws of EU member states, as well as privacy laws in other countries in which we operate, could lead to government enforcement actions and significant sanctions or penalties against us, adversely impact our results of operations and subject us to negative publicity.

The EU Data Protection Regulation, which will replace the current EU Data Protection Directive, was adopted in 2016 and will become enforceable on May 25, 2018. The EU Data Protection Regulation will introduce new data protection requirements in the EU and substantial fines for breaches of the data protection rules, may increase our responsibility and liability in relation to personal data that we process and may require us to put in place additional mechanisms to ensure compliance with the new EU data protection rules.

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."

Some of the provisions of the ACA have yet to be fully implemented, and there have been legal and political challenges to certain aspects of the ACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018 (BBA), among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". We continue to evaluate how the ACA and recent efforts to repeal and replace or limit the implementation of the ACA will impact our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 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. This includes aggregate reductions of Medicare payments to providers of 2 percent per fiscal year. These reductions went into effect on April 1, 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. Moreover, 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 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. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. 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 have increasingly passed legislation and implemented 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. 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.

Our employees, independent contractors, principal investigators, CROs, consultants or vendors may engage in misconduct or other improper activities, including noncompliance 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 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 product clinical manufacturing development, 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. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. 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 existing 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. We do not expect to be a PFIC for our current taxable year or in the future; however, our status as a PFIC is determined annually and subject to change. 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." The proceeds from this offering will be a passive asset under these rules and could cause us to meet the PFIC Asset Test for our taxable year that includes this offering. If we are a PFIC in any taxable year in which you hold shares and you are a "U.S. Holder" (as described in the section of this prospectus titled "Taxation—Material U.S. Federal Income Tax Considerations for U.S. Holders"), we always will be a PFIC with respect to your shares. If we are a PFIC and you are a U.S. Holder and do not make a mark-to-market election (discussed below) with respect to our ordinary shares, you 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 adverse tax consequences could be materially adverse to you.

If you are a U.S. Holder and make a valid, timely mark-to-market election with respect to our ordinary shares, you will recognize as ordinary income or loss in each year that we meet the PFIC Income Test or PFIC Asset Test an amount equal to the difference between your 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. See the section of this prospectus titled "Taxation—Material U.S. Federal Income Tax Considerations for U.S. Holders—Passive Foreign Investment Company Consequences" for a discussion of the PFIC and mark-to-market rules.

We do not expect to provide U.S. Holders with the information necessary for a U.S. Holder to make a qualified electing fund, or "QEF election," under the U.S. federal income tax laws, and prospective investors should assume that a QEF election will not be available.

If the IRS determines that we are not a PFIC, and you previously paid taxes pursuant to a mark-to-market election, you may have paid more taxes than you 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 you previously paid taxes pursuant to a mark-to-market election, then you may have paid more taxes than you legally owed due to such election. If you do not, or are not able to, file a refund claim before the expiration of the applicable statute of limitations, you 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.

On December 22, 2017, U.S. President Donald Trump signed into law a bill that enacts comprehensive changes to the U.S. federal income tax system. This law and related future legislation, regulations and rulings could affect the U.S. federal income tax treatment of us and U.S. Holders of our ordinary shares. You should consult your tax advisors regarding such changes and their potential impact related to an investment in our ordinary shares.

A future transfer of your 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. However, if you hold your ordinary shares directly rather than beneficially through DTC, any transfer of your 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. See "Irish Tax Considerations—Stamp Duty" for more information.

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

As noted elsewhere in this prospectus, 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 (currently at a rate of 20%) 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 would include the United States, should generally be entitled to exemptions from dividend withholding tax provided that the appropriate documentation is in place. See the section titled "Irish Tax Considerations—Withholding Tax on Dividends Paid on Our Ordinary Shares" for more information and, in particular, please note the requirement to complete certain dividend withholding tax forms in order to qualify for many of the exemptions.

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

As noted elsewhere in this prospectus, 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 (for example, they are resident in Ireland). 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. See the section titled "Irish Tax Considerations—Income Tax on Dividends Paid on Our Ordinary Shares."

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. Gifts and inheritances passing between spouses are exempt from CAT. Children have a tax-free threshold of €310,000 in respect of taxable gifts or inheritances received from their parents. See the section titled "Irish Tax Considerations—Capital Acquisitions Tax" for more information.

Risks Related to this Offering and Our Ordinary Shares

No active market for our ordinary shares exists or may develop, and you may not be able to resell your ordinary shares at or above the initial public offering price.

Prior to this offering, there has been no public market for our ordinary shares, and an active public market for our ordinary shares may not develop or be sustained after this offering. We and the representatives of the underwriters have determined the initial public offering price of our ordinary shares by arm's-length negotiations, and the initial public offering price does not necessarily reflect the price at which investors in the market will be willing to buy and sell our ordinary shares following this offering. In addition, an active trading market may not develop following completion of this offering or, if it is developed, may not be sustained. The lack of an active market may impair your ability to sell your ordinary shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also adversely affect our ability to raise capital by selling securities in the future, or impair our ability to in-license or acquire other product candidates, businesses or technologies using our ordinary shares as consideration.

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

If a market for our ordinary shares develops following this offering, 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. These factors include those discussed elsewhere in this "Risk Factors" section of this prospectus and others, such as:

- results from, and any delays in, our current and future clinical trials, in particular our 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 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.

We do not currently have research coverage by securities and industry analysts, and if no significant coverage is initiated or maintained following this offering, 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.

Upon the completion of this offering, based on shares outstanding as of March 31, 2018, our executive officers, directors, holders of 5% or more of our ordinary shares and their respective affiliates will beneficially own in the aggregate approximately 51.4% of our outstanding ordinary shares. The ownership percentage disclosed above does not reflect the purchase of any ordinary shares in this offering by these holders. 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 shareholders may feel are in their best interest.

We will have broad discretion regarding use of the net proceeds from this offering, and we may use them in ways that do not enhance our operating results or the market price of our ordinary shares.

Our management will have broad discretion regarding the use of the net proceeds from this offering, and we could spend the net proceeds in ways our shareholders may not agree with or that do not yield a favorable return, if any. We intend to use the net proceeds from this offering to initiate, complete enrollment, and produce top-line results relating to our three Phase 3 clinical trials and to make payments under the Pfizer License. We intend to use the remainder of the net proceeds from this offering for working capital and other general corporate purposes. We may also use a portion of the net proceeds to further pursue the establishment of additional sources for the manufacture of sulopenem tablets and IV vials or to acquire or in-license additional product candidates or complementary assets or businesses; however, we currently have no agreements, commitments or understandings to complete any such transaction. Our actual use of these proceeds may differ substantially from our current intentions. If we do not invest or apply the proceeds from this offering in ways that improve our operating results or our prospects, our share price could decline.

Purchasers in this offering will experience immediate and substantial dilution in the book value of their investment.

The initial public offering price of our ordinary shares is substantially higher than the pro forma net tangible book value per ordinary share before giving effect to this offering. Accordingly, if you purchase our ordinary shares in this offering, based on the midpoint range set forth on the cover of this prospectus and the issuance of 5,333,333 ordinary shares in this offering, we estimate that you will incur immediate dilution of approximately $5.02 per ordinary share, representing the difference between the price per share you pay for our ordinary shares and our pro forma as adjusted net tangible book value per ordinary share as of March 31, 2018. Furthermore, if the underwriters exercise their option to purchase additional shares, if outstanding stock options are exercised, if we issue awards to our employees under our equity incentive plans, or if we otherwise issue additional ordinary shares, you could experience further dilution. See the section titled "Dilution" for additional information.

If we raise additional capital in the future, your level of ownership in us 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 your rights as an 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 could cause our share price to fall.

If our existing shareholders sell, or indicate an intention to sell, substantial amounts of our ordinary shares in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the trading price of our ordinary shares could decline. Based upon the number of ordinary shares outstanding as of March 31, 2018, upon the completion of this offering, we will have 13,142,756 ordinary shares outstanding, assuming (i) the conversion of all outstanding preference shares into 7,396,313 ordinary shares, which we expect to automatically occur immediately prior to the completion of this offering, (ii) no exercise of the underwriters' option to purchase 799,999 additional ordinary shares and (iii) no exercise of options or warrants outstanding as of March 31, 2018. Of these outstanding ordinary shares, the 5,333,333 ordinary shares sold in this offering will be freely tradable, except that any ordinary shares acquired by our "affiliates" as that term is defined in Rule 144 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including any ordinary shares acquired by existing holders of our ordinary shares that have indicated an interest in purchasing ordinary shares in this offering, may only be sold if registered under the Securities Act or if such registration is not required, such as in compliance with Rule 144.

The remaining 7,809,423 ordinary shares are subject to lock-up agreements. The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. The representatives of the underwriters, however, may permit our shareholders who are subject to these lock-up agreements to sell their ordinary shares prior to the expiration of the lock-up agreements. After the lock-up agreements expire, these 7,809,423 ordinary shares will be eligible for sale in the public market, 6,751,348 of which shares are held by directors, executive officers and other affiliates (not taking into account any shares that may be purchased in this offering by existing holders of our ordinary shares) and will be subject to volume limitations under Rule 144 under the Securities Act.

In addition, 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, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If 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.

After this offering, the holders of 7,809,423 ordinary shares, or 100% of our total outstanding ordinary shares as of March 31, 2018, will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these shareholders could have an adverse effect on the trading price of our ordinary shares.

Participation in this offering by certain of our existing shareholders would reduce the available public float for our ordinary shares.

Certain of our directors and existing shareholders, or their affiliates, have indicated an interest in purchasing up to an aggregate of approximately $35.0 million of our ordinary shares in this offering. Assuming these holders of our ordinary shares were to purchase all of these ordinary shares, they, together with our executive officers, directors and other owners of 5% or more of our outstanding ordinary shares and their respective affiliates, would beneficially own, in the aggregate, approximately 69.1% of our outstanding ordinary shares after this offering, based on the number of shares outstanding as of March 31, 2018 and an initial public offering price at the midpoint range set forth on the cover of this prospectus.

If these holders of our ordinary shares were to purchase all or a portion of these ordinary shares, such purchases would reduce the available public float for our ordinary shares because such shareholders would be restricted from selling the shares by a lock-up agreement they have entered into with the underwriters and by restrictions under applicable securities laws. As a result, any purchase of ordinary shares by such shareholders in this offering may reduce the liquidity of our ordinary shares relative to what it would have been had these shares been purchased by investors that were not affiliated with us.

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

You 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 you 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 you 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.

You 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. For further information with respect to your rights as a holder of our ordinary shares, see “Description of Share Capital.”

As a newly public company, we will incur significant additional costs, and our management will be required to devote substantial time and attention to our public reporting obligations.

As a publicly-traded company, we will 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 presenting only two years of audited financial statements and related financial disclosure, 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 the completion of this initial public offering), 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 December 31, 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 will be subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of the applicable listing standards of the Nasdaq Global Market. We expect that the requirements of these rules and regulations will continue to increase our legal, accounting and financial compliance costs, make some activities more difficult, time-consuming and costly and place significant strain on our personnel, systems and resources. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are continuing to develop and refine our disclosure controls and other procedures that are designed to ensure that information required to be disclosed by us in the reports that we will file with the SEC is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms and that information required to be disclosed in reports under the Exchange Act is accumulated and communicated to our principal executive and financial officers. We are also continuing to improve our internal control over financial reporting. In order to develop, maintain and improve the effectiveness of our disclosure controls and procedures and internal control over financial reporting, we have expended, and anticipate that we will continue to expend, significant resources, including accounting-related costs and significant management oversight.

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. We are not currently required to comply with the SEC rules that implement Section 404 of the Sarbanes-Oxley Act and are therefore not required to make a formal assessment of the effectiveness of our internal control over financial reporting for that purpose. As a public company, we will be required to provide an annual management report on the effectiveness of our internal control over financial reporting commencing with our second annual report on Form 10-K.

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 to achieve a return on your investment in our company is expected to be if the market price of our ordinary shares appreciates and you sell your ordinary shares at a profit. The price of our ordinary shares prevailing in the market after this offering may not exceed the price that you pay.

Anti-takeover provisions in our Articles 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 will 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 will 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 additional 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.

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 Nasdaq, we will become 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. Following the authorization for trading of our ordinary shares on Nasdaq, under the Irish Takeover Rules, certain separate concert parties will be 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. Following the listing of our ordinary shares on Nasdaq, 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. For a description of certain takeover provisions applicable to us, see the section titled "Description of Share Capital—Irish Takeover Rules and Substantial Acquisition Rules." Accordingly, the application of the Irish Takeover Rules may restrict the ability of certain of our shareholders and directors to acquire our ordinary shares.

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 adopted on closing of this offering will contain, 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this prospectus 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 the net proceeds from this offering;
- 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 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;
- 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 and/or collaborations and the potential benefits of such arrangements;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- 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 prospectus. 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 prospectus 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 prospectus to conform these statements to new information, actual results or to changes in our expectations, except as required by law.

You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement of which this prospectus is a part 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 prospectus 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 prospectus, 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.

USE OF PROCEEDS

We estimate that the net proceeds from the sale of 5,333,333 ordinary shares in this offering will be approximately $71.4 million, based on an assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option to purchase additional ordinary shares from us, we estimate that our net proceeds will be approximately $82.6 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per share would increase (decrease) our net proceeds by $5.0 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) by 1,000,000 shares in the number of shares offered by us would increase (decrease) the net proceeds from this offering by $14.0 million, assuming the assumed initial public offering price remains the same, after deducting the estimated underwriting discounts and commissions. The information discussed above is illustrative only and will adjust based on the actual initial public offering price and other terms of this offering determined at pricing. Any increase or decrease in the net proceeds would not change our intended use of proceeds.

We estimate that we will use the net proceeds from this offering, together with our cash, cash equivalents, short-term investments and available borrowing under our credit facility, as follows:

- approximately $65.0 million to fund our Phase 3 clinical trials of oral sulopenem and sulopenem in three indications;
- approximately $15.0 million for milestone payments to Pfizer Inc. payable upon commencement of Phase 3 clinical development for oral sulopenem and sulopenem pursuant to the exclusive license agreement we have entered into with Pfizer; and
- the balance for working capital and other general corporate purposes, including regulatory, manufacturing, clinical supply and related costs.

We believe the anticipated net proceeds from this offering, together with our existing cash, cash equivalents, short-term investments and available borrowing under our credit facility, will enable us to complete our three planned Phase 3 clinical trials. However, we expect that we will require additional capital to submit our applications to regulatory agencies and to commercialize oral sulopenem and sulopenem, if we receive regulatory approval.

The expected use of proceeds from this offering represent our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors and any unforeseen cash needs. As a result, management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in interest-bearing, investment-grade securities, certificates of deposit or government securities.

DIVIDEND POLICY

We have never declared or paid dividends on our ordinary shares. We currently intend to retain all available funds and any future earnings to support operations and to finance the growth and development of our business. In addition, our ability to pay dividends is currently restricted by the terms of our credit facility with Silicon Valley Bank. We do not intend to declare or pay cash dividends on our ordinary shares in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors subject to applicable laws (including the Irish Companies Act, which requires, inter alia, Irish companies to have profits available for distribution equal to or greater than the amount of the proposed dividend), and will depend upon, among other factors, our results of operations, financial condition, contractual restrictions and capital requirements. Our future ability to pay cash dividends on our shares may be limited by the terms of any future debt or preferred securities.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and short-term investments and capitalization as of March 31, 2018:

- on an actual basis;
- on a pro forma basis, to reflect: (1) the conversion of all outstanding preferred shares into 7,396,313 of our ordinary shares immediately prior to the closing of this offering, (2) the drawdown of $15.0 million under our credit facility with Silicon Valley Bank in April 2018, and (3) the filing and effectiveness of our amended and restated constitution in connection with the closing of this offering; and
- on a pro forma as adjusted basis, to further reflect the sale by us of 5,333,333 ordinary shares in this offering at an assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the information in this table together with our consolidated financial statements and related notes included elsewhere in this prospectus and the sections titled "Selected Consolidated Financial and Other Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	As of March 31, 2018		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
	(in thousands, except share and per share data)		
Cash, cash equivalents, restricted cash and short-term investments	$ 59,754	$ 74,754	$ 146,154
Credit facility	—	15,000	15,000
Convertible preferred shares, $0.01 par value; 7,833,956 shares authorized, 7,396,313 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	74	—	—
Shareholders' equity:			
Preferred shares, $0.01 par value; no shares authorized, issued or outstanding, actual; no shares authorized and no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	—
Ordinary shares, $0.01 par value; 44,557,606 shares authorized, 413,110 shares issued and outstanding, actual; 50,000,000 shares authorized, 7,809,423 shares issued and outstanding, pro forma; 50,000,000 shares authorized, 13,142,756 shares issued and outstanding, pro forma as adjusted	4	78	131
Additional paid-in capital	126,535	126,535	197,882
Accumulated deficit	(66,883)	(66,883)	(66,883)
Total shareholders' equity	59,656	59,730	131,130
Total capitalization	59,730	74,730	146,130

(1) Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) each of cash, cash equivalents, and short-term investments, additional paid-in capital, total shareholders' equity, and total capitalization by $5.0 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of 1,000,000 shares in the number of shares offered by us would increase (decrease) cash, cash equivalents, and short-term investments, additional paid-in capital, total shareholders' equity, and total capitalization by $14.0 million, assuming the assumed initial public offering price remains the same, after deducting the estimated underwriting discounts and commissions. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

The number of ordinary shares to be outstanding after this offering is based on 7,809,423 ordinary shares outstanding as of March 31, 2018 and excludes:

- 248,128 ordinary shares issuable upon the exercise of outstanding stock options as of March 31, 2018, with a weighted-average exercise price of $3.31 per share;
- 194,901 ordinary shares reserved for future issuance under our 2015 Equity Incentive Plan as of March 31, 2018; all shares reserved for future issuance and not subject to an outstanding stock option will cease to be available for issuance at the time our 2018 Equity Incentive Plan becomes effective in connection with this offering;
- 1,018,459 ordinary shares reserved for future issuance under our 2018 Equity Incentive Plan, as well as any increases in the number of ordinary shares reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement for this offering. Of the 1,018,459 ordinary shares reserved for future issuance under our 2018 Equity Incentive Plan, upon the execution of the underwriting agreement for this offering, options to purchase 417,867 ordinary shares will be granted to our employees and additional options and/or restricted stock units will be granted to our non-employee directors; and
- 19,890 ordinary shares issuable upon exercise of outstanding warrants issued subsequent to March 31, 2018 at a price of $18.85 per share.

DILUTION

If you invest in our ordinary shares in this offering, your interest will be diluted to the extent of the difference between the initial public offering price per ordinary share and the pro forma as adjusted net tangible book value per ordinary share after the closing of the offering.

Our pro forma net tangible book value as of March 31, 2018 was $59.7 million, or $7.65 per share. Pro forma net tangible book value per share is determined by subtracting our total liabilities from the total book value of our tangible assets and dividing the difference by the number of ordinary shares deemed to be outstanding at that date, after giving effect to (i) the conversion of all outstanding preferred shares into an aggregate of 7,396,313 ordinary shares immediately prior to the closing of this offering; and (ii) the drawdown of $15.0 million under our credit facility with Silicon Valley Bank in April 2018.

After giving effect to the sale of 5,333,333 ordinary shares in this offering at an assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2018, would have been $131.1 million, or $9.98 per share. This represents an immediate increase in pro forma as adjusted net tangible book value of $2.33 per share to our existing shareholders and immediate dilution of $5.02 per share to investors purchasing ordinary shares in this offering.

The following table illustrates this dilution on a per share basis to investors purchasing shares in this offering:

Assumed initial public offering price per share		$15.00
Pro forma net tangible book value per share as of March 31, 2018	$7.65	
Increase in pro forma net tangible book value per share attributable to investors purchasing shares in this offering	2.33	
Pro forma as adjusted net tangible book value per share after this offering		9.98
Dilution in net tangible book value per share to investors purchasing shares in this offering		$ 5.02

Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per share would increase (decrease) our pro forma as adjusted net tangible book value per share after this offering by $0.38 per share and the dilution to investors purchasing shares in this offering by $0.62 per share, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase of 1,000,000 shares in the number of ordinary shares offered by us would increase the pro forma as adjusted net tangible book value by $0.28 per share and decrease the dilution to investors by $0.28 per share, assuming the assumed initial public offering price remains the same and after deducting the estimated underwriting discounts and commissions. Similarly, each decrease of 1,000,000 shares in the number of ordinary shares offered by us would decrease the pro forma as adjusted net tangible book value by $0.33 per share and increase the dilution to investors purchasing shares in this offering by $0.33 per share, assuming the assumed initial public offering price remains the same and after deducting the estimated underwriting discounts and commissions.

The following table summarizes, as of March 31, 2018, on the pro forma as adjusted basis described above:

- the total number of ordinary shares purchased from us by our existing shareholders and by investors purchasing shares in this offering;
- the total consideration paid to us by our existing shareholders and by investors purchasing shares in this offering, assuming an initial public offering price of $15.00 per share, the midpoint of the range set forth on the cover page of this prospectus, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us; and

- the average price per share paid by existing shareholders and by investors purchasing shares in this offering.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing shareholders	7,809,423	59.4%	$ 125,738,633	61.1%	$ 16.10
Investors participating in this offering	5,333,333	40.6	79,999,995	38.9	$ 15.00
Total	13,142,756	100.0%	$205,738,628	100.0%	$15.65

A $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per share would increase (decrease) the total consideration paid to us by investors participating in this offering by $5.3 million assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and before deducting the estimated underwriting discounts and commissions and estimated expenses payable by us.

The tables and calculations above are based on 7,809,423 ordinary shares outstanding as of March 31, 2018, and exclude:

- 248,128 ordinary shares issuable upon the exercise of outstanding stock options as of March 31, 2018, with a weighted-average exercise price of $3.31 per share;
- 194,901 ordinary shares reserved for future issuance under our 2015 Equity Incentive Plan as of March 31, 2018; all shares reserved for future issuance and not subject to an outstanding stock option will cease to be available for issuance at the time our 2018 Equity Incentive Plan becomes effective in connection with this offering;
- 1,018,459 ordinary shares reserved for future issuance under our 2018 Equity Incentive Plan, as well as any increases in the number of ordinary shares reserved for future issuance under this plan, which will become effective upon the execution of the underwriting agreement for this offering. Of the 1,018,459 ordinary shares reserved for future issuance under our 2018 Equity Incentive Plan, upon the execution of the underwriting agreement for this offering, options to purchase 417,867 ordinary shares will be granted to our employees and additional options and/or restricted stock units will be granted to our non employee directors; and
- 19,890 ordinary shares issuable upon exercise of outstanding warrants issued subsequent to March 31, 2018 at a price of $18.85 per share.

To the extent any outstanding options are exercised, new options are issued under our equity incentive plans, or we issue additional ordinary shares in the future, there will be further dilution to investors participating in this offering. If all outstanding options as of March 31, 2018 and warrants issued subsequent to March 31, 2018 were exercised, then our existing shareholders, including the holders of these options and warrants would own 60.2% and investors participating in this offering would own 39.8% of the total number of ordinary shares outstanding upon the closing of this offering.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the selected consolidated financial data below in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements, related notes, and other financial information included elsewhere in this prospectus. The selected consolidated financial and other data in this section are not intended to replace the consolidated financial statements and are qualified in their entirety by the consolidated financial statements and related notes included elsewhere in this prospectus.

The following selected consolidated statements of operations data for the years ended December 31, 2016 and 2017 and selected consolidated balance sheet data as of December 31, 2017 have been derived from our audited consolidated financial statements included elsewhere in this prospectus. The consolidated statements of operations data for the three months ended March 31, 2017 and 2018 and the consolidated balance sheet data as of March 31, 2018 are derived from our unaudited interim consolidated financial statements included elsewhere in this prospectus. Our unaudited interim consolidated financial statements were prepared on a basis consistent with our audited consolidated financial statements and include, in our opinion, all adjustments, consisting only of normal recurring adjustments, that we consider necessary for a fair presentation of the financial information set forth in those statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in any future period, and the results for the three months ended March 31, 2018 are not necessarily indicative of the results to be expected for the full year or any other period.

	Year Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
			(unaudited)	
	(in thousands, except share and per share data)			
Consolidated Statements of Operations Data:				
Revenue	$ —	$ 508	$ —	$ 191
Operating expenses:				
Research and development	(10,101)	(25,499)	(4,534)	(10,879)
General and administrative	(3,258)	(4,464)	(1,008)	(1,515)
Total operating expenses	(13,359)	(29,963)	(5,542)	(12,394)
Operating loss	(13,359)	(29,455)	(5,542)	(12,203)
Interest income, net	—	277	—	85
Other income/(expense), net	8	216	(68)	61
Total other income	8	493	(68)	146
Loss before income taxes	(13,351)	(28,962)	(5,610)	(12,057)
Income tax expense	(113)	(444)	(227)	(89)
Net loss and comprehensive loss	(13,464)	(29,406)	(5,837)	(12,146)
Net loss attributable to ordinary shareholders	$(13,464)	$ (29,406)	$ (5,837)	$ (12,146)
Net loss per share attributable to ordinary shareholders, basic and diluted(1)	$(568.87)	$ (170.84)	$(103.68)	$ (61.36)
Weighted average ordinary shares outstanding, basic and diluted	23,668	172,130	56,301	197,949
Pro forma net loss per share attributable to ordinary shareholders (unaudited)		$ (5.02)		$ (1.60)
Pro forma weighted average ordinary shares outstanding, basic and diluted (unaudited) (2)		5,858,793		7,594,262

(1) Net loss per share, basic and diluted is the same due to our net loss.

(2) Assumes automatic conversion of all shares of convertible preferred shares into ordinary shares at a 1:1 conversion rate.

	As of December 31,		As of March 31,
	2016	2017	2018
		(in thousands)	
Consolidated Balance Sheet Data:			
Cash, cash equivalents, restricted cash and short-term investments	$24,809	$39,216	$ 59,754
Working capital(1)	21,643	37,047	57,062
Total assets	26,917	46,757	68,131
Total liabilities	4,219	7,206	8,401
Convertible preferred shares	30	57	74
Total shareholders' equity	22,668	39,494	59,656

(1) Working capital is equal to current assets minus current liabilities.

Recent Developments

In April 2018, we entered into a secured credit facility with Silicon Valley Bank and made an initial drawdown of $15 million.

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 the section titled "Selected Consolidated Financial Data" and our consolidated financial statements and the related notes appearing at the end of this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, 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 prospectus, our actual results could differ materially from the results described in or implied by these forward-looking statements.

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 successfully developed sulopenem in an oral tablet formulation, sulopenem etzadroxil-probenecid, which we refer to herein as oral sulopenem. Both sulopenem products 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, resistant infections. Therefore, we plan to initiate a Phase 3 clinical program in the second half of 2018 for the treatment of adults in three indications: uUTI, complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (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 intend to conduct the Phase 3 clinical trials under Special Protocol Assessment (SPA) agreements from the FDA. We expect to complete enrollment and produce topline data for all three clinical trials in the second half of 2019, and submit our new drug applications (NDAs) to the FDA by the end of 2019.

Since our inception in June 2015, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, establishing a supply chain, planning for commercialization, and conducting research and development activities for our sulopenem program. We do not have any products approved for sale and have not generated any revenue from product sales. In June 2017, we were granted a sub-award of up to $1.5 million from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) program (the CARB-X Award). The CARB-X Award supports preclinical and clinical trials in support of our potential regulatory filings for oral sulopenem and sulopenem, along with chemistry, manufacturing and controls optimization and development of our commercial bilayer tablet. We have funded our operations to date primarily with proceeds from the sale of preferred shares and ordinary shares and payments received under the funding arrangement with CARB-X. Through March 31, 2018, we had received gross cash proceeds of $119.6 million from sales of our preferred shares and ordinary shares. In April 2018, we entered into a secured credit facility with Silicon Valley Bank (SVB) and made an initial drawdown of $15.0 million.

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). We have developed an oral formulation, sulopenem etzadroxil-probenecid combined in a single bilayer tablet. We

refer to sulopenem delivered intravenously as sulopenem and, together with oral sulopenem, as our sulopenem program. Under an exclusive license agreement with Pfizer (the Pfizer License), we paid Pfizer a one-time nonrefundable upfront fee of $5.0 million and are obligated to pay Pfizer potential future clinical and 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 (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 based on marginal net sales of each licensed product. Pfizer also received 381,922 Series A preferred shares as additional payment for the licensed rights. In addition, if we sublicense or assign our rights to 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.

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. Our net losses for 2016 and 2017 were $13.5 million and $29.4 million, respectively. Our net losses for the three months ended March 31, 2017 and 2018 were $5.8 million and $12.1 million, respectively. As of March 31, 2018, we had an accumulated deficit of $66.9 million. We expect to continue to incur significant expenses for at least the next two years as we advance our sulopenem program through Phase 3 clinical trials, seek regulatory approval and engage in market preparation 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 Furthermore, we may 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, upon the closing of this offering, we 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, 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 public or private 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, 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 March 31, 2018, we had cash, cash equivalents, restricted cash and short-term investments of $59.8 million. In April 2018, we entered into a secured credit facility with SVB and made an initial drawdown of $15.0 million. We believe that the anticipated net proceeds from this offering, together with our existing cash, cash equivalents, restricted cash short-term investments and available borrowings under our credit facility, will enable us to fund our operating expenses and capital expenditure requirements through the fourth quarter of 2019. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See the section titled “—Liquidity and Capital Resources.”

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 CARB-X Award. We expect that our revenue for the next few years will be derived primarily from payments under the CARB-X Award or 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 receive funding from CARB-X as we incur qualifying expenses. During the year ended December 31, 2017, we recognized $0.5 million of revenue under this award. During the three months ended March 31, 2018, we recognized $0.2 million 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 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, we expect that our research and development expenses will increase substantially over the next two years as we increase personnel costs, including share-based compensation, commence Phase 3 clinical trials for our sulopenem program, conduct other clinical trials and prepare regulatory filings for oral sulopenem and sulopenem. We also expect to incur additional expenses related to milestone and royalty payments payable to Pfizer with whom we have entered into the Pfizer License to acquire the rights to oral sulopenem and sulopenem.

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 that can be used in our clinical trials and 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. 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. For example, if we experience significant delays in enrollment in any of our planned clinical trials, or are required to add additional patients to a study to remain consistent with our original trial design assumptions, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate.

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 and administrative functions. General and administrative expenses also include director compensation and travel expenses and professional fees for legal, patent, consulting, accounting and audit services.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our 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. We anticipate the additional costs for these services will increase our general and administrative expenses by approximately $1.5 million to $2.0 million on an annual basis. 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.

Other Income (Expense)

Interest Income, Net

Interest income consists of interest earned and any unrealized gains or losses on our cash equivalents and short-term investments, which are invested in money market accounts. Our interest income has not been significant due to low interest earned on those balances.

Foreign Exchange Gain (Loss)

We realize foreign currency gains (losses) in the normal course of business based on movement in the applicable exchange rates. These gains (losses) have been insignificant to date and are included as a component of other income (expense).

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.

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 position 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 at the end of this prospectus, 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 and clinical studies; 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 based on the fair value on the date of the grant and recognize the corresponding compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. We have only issued share awards with service-based vesting conditions and record the expense for these awards using the straight-line method.

For share-based awards granted to consultants and non-employees, we recognize compensation expense over the period during which services are rendered by such consultants and non-employees 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.

We estimate the fair value of each share option grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our ordinary shares and assumptions we make for the volatility of our ordinary shares, the expected term of our share options, the risk-free interest rate for a period that approximates the expected term of our share options and our expected dividend yield.

Determination of the Fair Value of Ordinary Shares

As there has been no public market for our ordinary shares to date, the estimated fair value of our ordinary shares has been 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 IPO, or a sale of our company in light of prevailing market conditions; and
- the analysis of IPOs 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.

Following the closing of this offering, the fair value of our ordinary shares will be determined based on the quoted market price of our ordinary shares.

Grants of Share-based awards

The following table sets forth by grant date the number of ordinary shares subject to awards granted between November 18, 2015 and March 31, 2018, the per share exercise price of the options and the per share estimated fair value of the options utilized to calculate share-based compensation expense:

Date of Grant	Type of Award	Number of shares underlying awards granted	Exercise price per share	Fair value per share on grant date
3/8/2016	Option	19,096	$3.14	$1.80
5/25/2016	Option	6,365	3.14	1.80
8/15/2016	Option	9,547	3.14	1.80
12/7/2016	Option	14,322	3.14	1.80
3/24/2017	Option	14,320	3.30	1.88
6/6/2017	Option	3,182	3.30	1.88
9/12/2017	Option	170,794	3.30	1.88
12/5/2017	Option	10,502	4.40	2.50

The Board awarded 417,867 stock options to employees and additional stock options and/or restricted stock units to our non-employee directors on March 14, 2018 under the 2018 Plan. These options and/or restricted stock units will be granted and priced upon execution of the underwriting agreement related to the IPO.

Results of Operations

Comparison of the Years Ended December 31, 2016 and 2017

The following table summarizes our operating losses for the years ended December 31, 2016 and 2017:

	Year Ended December 31,		
	2016	2017	Change
	(in thousands)		
Revenue	$ —	$ 508	$ 508
Operating expenses:			
Research and development	$ 10,101	$ 25,499	$ 15,398
General and administrative	3,258	4,464	1,206
Total operating expenses	$ 13,359	$ 29,963	$ 16,604
Operating loss	(13,359)	(29,455)	(16,096)

Revenue

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

Research and Development Expenses

	Year Ended December 31,		
	2016	2017	Change
	(in thousands)		
Chemistry, manufacturing and control (CMC) related expenses	$ 4,030	$ 15,237	$ 11,207
CRO and other preclinical and clinical trial related expenses	2,894	4,665	1,771
Personnel related (including share-based compensation)	1,717	3,527	1,810
Consulting fees	1,460	2,070	610
Total research and development expenses	$ 10,101	$ 25,499	$ 15,398

The increase in CMC related expenses of $11.2 million was primarily due to formulation development, manufacturing process, and manufacturing of clinical trial material in anticipation of our Phase 3 clinical trials in the second half of 2018. CRO and other preclinical and clinical trial related expenses increased by $1.8 million due to increased Phase 1 and Phase 4 clinical trial activity. Personnel related costs increased by $1.8 million as a result of an increase in headcount in our CMC, clinical development and regulatory functions. Personnel related costs for the years ended December 31, 2016 and 2017 included share-based compensation expense of $0.1 million and $0.1 million, respectively. The increase in consulting fees of $0.6 million was primarily due to the increase in consultants used for preclinical and clinical trial activity.

General and Administrative Expenses

	Year Ended December 31,		
	2016	2017	Change
	(in thousands)		
Personnel related (including share-based compensation)	$ 2,003	$ 2,463	$ 460
Professional and consultant fees	903	929	26
Facility related and other	352	1,072	720
Total general and administrative expenses	$ 3,258	$ 4,464	$ 1,206

The increase in facility related and other costs of $0.7 million was primarily due to the lease of office space in Dublin that we entered into at the end of 2016, software costs, director compensation and travel expenses, and general support costs for the increase in headcount. Personnel-related costs increased by $0.5 million as a result of an increase in headcount in our general and administrative function. Personnel related costs for the years ended December 31, 2016 and 2017 included share-based compensation expense of $0.2 million and $0.3 million, respectively.

Comparison of the Three Months Ended March 31, 2017 and 2018

The following table summarizes our operating losses for the three months ended March 31, 2017 and 2018:

	Three Months Ended March 31,		
	2017	2018	Change
	(in thousands)		
Revenue	$ —	$ 191	$ 191
Operating expenses:			
Research and development	$ 4,534	$ 10,879	$ 6,345
General and administrative	1,008	1,515	507
Total operating expenses	$ 5,542	$ 12,394	$ 6,852
Operating loss	(5,542)	(12,203)	(6,661)

Revenue

In June 2017, CARB-X awarded us funds of up to $1.5 million to advance the development of our sulopenem program. We receive funding from CARB-X as we incur qualifying expenses. During the three months ended March 31, 2018, we recognized $0.2 million of revenue under this award.

Research and Development Expenses

	Three Months Ended March 31,		
	2017	2018	Change
	(in thousands)		
Chemistry, manufacturing and control (CMC) related expenses	$ 1,479	$ 6,670	$ 5,191
CRO and other preclinical and clinical trial related expenses	1,956	2,002	46
Personnel related (including share-based compensation)	649	1,971	1,322
Consulting fees	450	236	(214)
Total research and development expenses	$ 4,534	$ 10,879	$ 6,345

The increase in CMC related expenses of $5.2 million was primarily due to formulation development, manufacturing process, and manufacturing of clinical trial material in anticipation of our Phase 3 clinical trials in the second half of 2018. CRO and other preclinical and clinical trial related expenses remained flat period over period at approximately $2.0 million. Personnel related costs increased by $1.3 million as a result of an increase in headcount in our CMC, clinical development and regulatory functions. Personnel related costs for the three months ended March 31, 2017 and 2018 included share-based compensation expense of $0.0 million and $0.1 million, respectively. The decrease in consulting fees of $0.2 million was primarily due to the increase in headcount.

General and Administrative Expenses

	Three Months Ended March 31,		
	2017	2018	Change
	(in thousands)		
Personnel related (including share-based compensation)	$ 551	$ 906	$ 355
Professional and consultant fees	177	299	122
Facility related and other	280	310	30
Total general and administrative expenses	$ 1,008	$ 1,515	$ 507

Personnel-related costs increased by $0.4 million as a result of an increase in headcount in our general and administrative function. Personnel related costs for the three months ended March 31, 2017 and 2018 included share-based compensation expense of $0.1 million and $0.1 million, respectively. Professional and consultant fees increased by $0.1 million due to pre-commercialization activities. Facility related and other costs remained flat period over period at approximately $0.3 million.

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 and payments received under the funding arrangement with CARB-X. Through March 31, 2018, we had received gross cash proceeds of $119.6 million from sales of our Series A and Series B preferred shares and ordinary shares. As of March 31, 2018, we had cash, cash equivalents, restricted cash and short-term investments of $59.8 million.

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 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 available on closing and the other $15.0 million is available at our option upon the satisfaction of certain draw requirements: (i) the achievement of both primary endpoints from our Phase 3 uUTI trial and reporting satisfactory safety data; 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. A non-utilization fee of 1.5% of the aggregate undrawn principal amount shall apply if we satisfy the second draw requirements but choose not to draw down the second term loan. The principal borrowed under the secured credit facility bears interest 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, which interest is payable monthly in arrears.

The initial draw will require monthly amortization payments commencing November 1, 2019, which will be extended to April 1, 2020 if the second draw is made. All outstanding principal, plus a 4.2% final interest payment, will be due and payable on March 1, 2022 (Maturity Date).

The secured credit facility draws are subject to prepayment fees in the event of prepayment at any time prior to the Maturity Date.

In connection with the initial $15.0 million draw, we issued to SVB and Life Sciences Fund II LLC (LSF) warrants to purchase 19,890 Series B-2 preferred shares at an exercise price of $18.85 per share. If we draw down the second term loan, each of SVB and LSF will be entitled, pursuant to additional share warrants issued to

each of them at closing, to purchase such number of additional ordinary shares in an aggregate amount equal to 2.5% of the funded amount, 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.

Cash Flows

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

	Year Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
			(unaudited)	
	(in thousands)			
Net cash used in operating activities	$(11,298)	$(30,604)	$(5,435)	$(11,640)
Net cash (used in)/provided by investing activities	—	(31,587)	(518)	9,357
Net cash provided by financing activities	20,851	45,867	—	32,176
Net increase (decrease) in cash	$ 9,553	$(16,324)	$(5,953)	$ 29,893

Operating Activities

During the three months ended March 31, 2017, operating activities used $5.4 million of cash, resulting from our net loss of $5.8 million, partially offset by net cash provided by changes in our operating assets and liabilities of $0.3 million and non-cash charges of $0.1 million. Net cash provided by changes in our operating assets and liabilities for the three months ended March 31, 2017 consisted primarily of increases in accrued expenses related to clinical trial expenses and clinical trial supply costs, partially offset by an increase in prepaid expenses and other assets primarily related to advance payments to contract manufacturing organizations and a reduction in accounts payable.

During the three months ended March 31, 2018, operating activities used $11.6 million of cash, resulting from our net loss of $12.1 million, partially offset by net cash provided by changes in our operating assets and liabilities of $0.3 million and non-cash charges of $0.2 million. Net cash provided by changes in our operating assets and liabilities for the three months ended March 31, 2018 consisted primarily of increases in accrued expenses and accounts payable primarily due to increases in clinical trial expenses and clinical trial supply costs, partially offset by increases in prepaid expenses and other assets primarily related to professional fees associated with the initial public offering.

During the year ended December 31, 2016, operating activities used $11.3 million of cash, resulting from our net loss of $13.5 million, partially offset by non-cash charges of $0.4 million and net cash provided by changes in our operating assets and liabilities of $1.8 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2016 consisted primarily of increases in accrued expenses and accounts payable primarily due to increases in clinical trial supply and costs, partially offset by increases in prepaid expenses and other assets primarily related to advance payments to contract manufacturing organizations.

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 in changes in our operating assets and liabilities of $1.6 million, partially offset by non-cash charges of $0.4 million. Net cash used in 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 contract manufacturing organizations, partially offset by increases in accrued expenses and accounts payable primarily due to increases in clinical trial supply and costs.

Investing Activities

During the three months ended March 31, 2017, net cash used in investing activities of $0.5 million was primarily related to fixed asset purchases.

During the three months ended March 31, 2018, net cash provided by investing activities of $9.4 million was primarily related to sales of short-term investments of $15.8 million, partially offset by purchases of short-term investments of $6.4 million.

We did not use any cash for investing activities during the year ended December 31, 2016. During the year ended December 31, 2017, net cash used in investing activities of $31.6 million was primarily 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 three months ended March 31, 2018, net cash provided by financing activities was $32.2 million and consisted of net cash proceeds from the issuance of Series B-2 preferred shares in February 2018.

During the year ended December 31, 2016, net cash provided by financing activities was $20.9 million, and consisted of gross cash proceeds from the issuance of Series A preferred shares in December 2016.

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 our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the clinical trials of oral sulopenem and sulopenem. In addition, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Our expenses will also increase if and as we:

- conduct additional clinical trials for oral sulopenem and sulopenem, which include our planned Phase 1 clinical trials, which we expect will occur in 2018 and 2019, and our three planned pivotal Phase 3 clinical trials, which we plan to initiate in the second half of 2018;
- 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;
- 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 transition to a public reporting company; and
- acquire or in-license other product candidates or technologies.

We believe that the anticipated net proceeds from this offering, together with our existing cash, cash equivalents, restricted cash, short-term investments and available borrowings under our credit facility, will enable us to fund our operating expenses and capital expenditure requirements through the fourth quarter of 2019. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. We expect that we will require additional capital to file with regulatory agencies and commercialize oral sulopenem and sulopenem, if we receive regulatory approval, and to pursue in-licenses or acquisitions of other product candidates. If we receive regulatory approval for oral sulopenem or sulopenem, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize.

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 planned clinical trials of oral sulopenem and sulopenem;
- 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 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, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as an ordinary shareholder. 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 imposes 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 and

incur additional indebtedness, 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, 2017 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	4 to 5 Years	More than 5 Years
	(in thousands)				
Operating lease commitments(1)	$3,692	$ 487	$954	$894	$ 1,357
Total	$3,692	$ 487	$954	$894	$ 1,357

(1) Reflects payments due for our leases of office space under operating lease agreements that expire in 2018, 2022 and 2026.

Under our license agreement with Pfizer, we have agreed to make certain clinical, 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 expect to use $15.0 million of the proceeds from this offering for milestone payments to Pfizer. 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 $3.0 million to the supplier to acquire equipment, which will be used solely to manufacture product for us. This payment will be offset against the price of the product to be supplied under a future supply agreement. As of December 31, 2017, $0.6 million remained outstanding to the supplier.

In March 2018, we entered into an operating lease agreement for office space in Chicago for a period of five years that commences in June 2018. The aggregate lease payments over the five-year lease term are approximately $1.4 million.

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.

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 at the end of this prospectus.

Quantitative and Qualitative Disclosures about Market Risks

We had cash and cash equivalents of $38.3 million as of March 31, 2018, consisting of cash in non-interest bearing accounts in highly rated financial institutions in the United States and Ireland and money market accounts.

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, 2016 and 2017 and March 31, 2018, substantially all of our liabilities were denominated in U.S. dollars. Net foreign currency gains and losses did not have a material effect on our results of operations for the years ended December 31, 2016 and 2017 or the three months ended March 31, 2017 and 2018.

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.

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 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. Therefore, we plan to initiate a Phase 3 clinical program in the second half of 2018 for the treatment of adults in three indications: uUTI, complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (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 intend to conduct the Phase 3 clinical trials under Special Protocol Assessment (SPA) agreements from the FDA. We expect to complete enrollment and produce top-line data for all three clinical trials in the second half of 2019, and to submit our new drug applications (NDAs) to the FDA by the end of 2019.

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 will be 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 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, those 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.

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 build a commercial infrastructure to launch both product candidates in the United States. Data from a study we commissioned in 2017 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 plan to employ a dual sourcing strategy for critical elements of our sulopenem supply chain. 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 by the end of 2019. 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.

Sulopenem etzadroxil has an issued composition of matter patent in the United States (which we have exclusively licensed from Pfizer) that is scheduled to expire in 2029, subject to potential extension to 2034 under the Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Act). In addition, the FDA has designated sulopenem and oral sulopenem as Qualified Infectious Disease Products (QIDP) for the indications of uUTI, cUTI and cIAI pursuant to the Generating Antibiotic Incentives Now Act (the GAIN Act), which provides the potential for a more rapid NDA review cycle and could add five years to any regulatory exclusivity period that we may be granted. QIDP status for other indications, such as respiratory tract infections, gonorrhea and diabetic foot infection 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. None of our licensed patents cover the IV formulation of sulopenem.

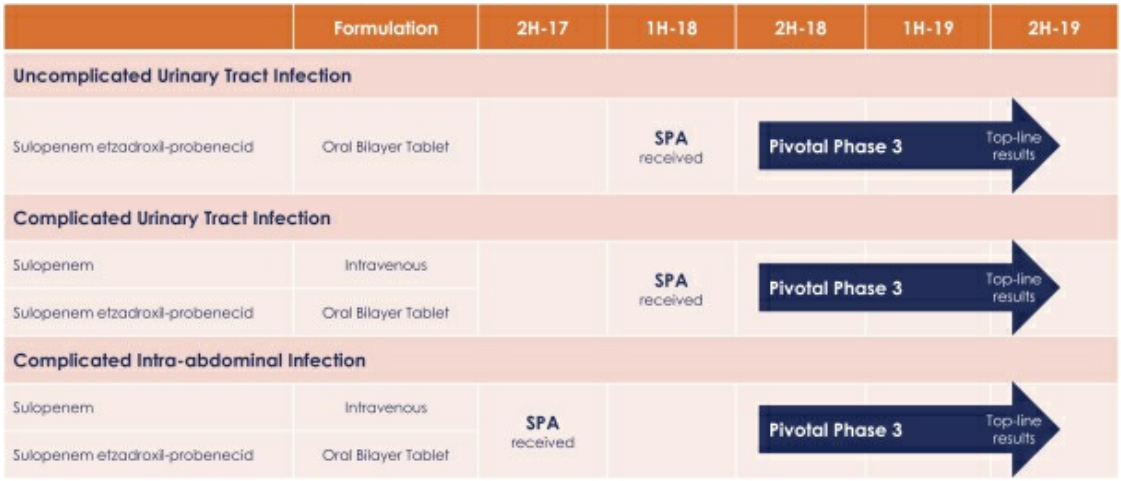
We were founded in June 2015 by former executives of Durata Therapeutics, Inc. (Durata), a biopharmaceutical company, which developed dalbavancin, another antibiotic from the Pfizer portfolio, and

successfully obtained FDA approval, launched the product in the United States, and submitted a marketing authorization application (MAA) to the EMA (approval was received in 2015). Durata was acquired by Allergan plc (formerly Actavis, Inc.) in late 2014. To date, we have raised approximately $120 million to develop our sulopenem program from a leading investor group including Advent Life Sciences LLP, Arix Bioscience plc, Bay City Capital LLC, Canaan Partners, Domain Associates L.L.C., Frazier Healthcare Partners, New Leaf Venture Partners, Pivotal bioVenture Partners, and Sofinnova Ventures, Inc., as well as our founders. Pfizer is also one of our shareholders.

Sulopenem Program, Clinical and Regulatory Status

We plan to pursue three initial indications for oral sulopenem and sulopenem, as summarized in the chart below. 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 FDA at an end of Phase 2 meeting, all supported by an advanced commercial manufacturing program which will provide clinical supplies.

We intend to conduct the Phase 3 clinical trials under SPA agreements from the FDA. We expect to complete enrollment and produce top-line data for all three clinical trials in the second half of 2019, and submit our NDAs to the FDA by the end of 2019.



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. We have received SPA agreements from the FDA for each of these trials. We plan to begin enrollment in all three clinical trials in the second half of 2018 and expect to conclude enrollment in the second half of 2019, with top-line data available in the same period.
- ***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 Phase 3 clinical trials are successful, we plan to submit NDAs for both oral sulopenem and sulopenem to the FDA by the end of 2019 and subsequently submit an MAA to the EMA.

- ***Maximize commercial potential of our sulopenem program.*** If approved, we intend to 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 respiratory tract infections, gonorrhea and diabetic foot 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.

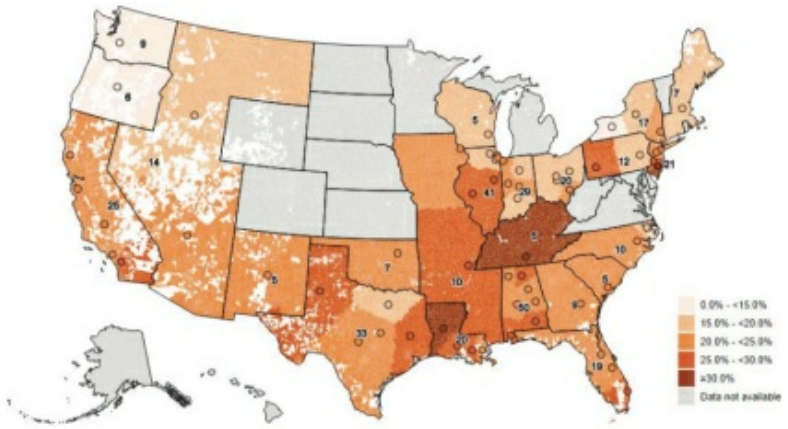
cIAIs have similar challenges to those of cUTIs. These complicated infections extend from a gastrointestinal source, such as the appendix or the colon, into the peritoneal space and can be associated with abscess formation.

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 given 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 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, those 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 has 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. 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, 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 confirmed after 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 ones 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.

Market Leader for Treatment of UTIs is Failing Patients

Fluoroquinolones are now the most widely used antibiotic class in treating community and hospital gram-negative infections. However, 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.

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 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, 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 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.
- ***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 active pharmaceutical ingredient (API) for oral sulopenem and sulopenem. Both of the contract manufacturers have the capability to produce vials for IV delivery. 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 transitioning to oral formulation upon discharge to complete therapy in the community setting; and
- treating cIAI with initiation of IV therapy in the hospital, and transitioning to oral formulation upon discharge 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 addition, cIAIs are the second most common cause of infectious mortality in intensive care units. Among approximately 350,000 cIAI patients in the United States each year, broad spectrum antibiotics are generally administered as first line treatment; treatment failure is more common due to the serious nature of these infections.

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.

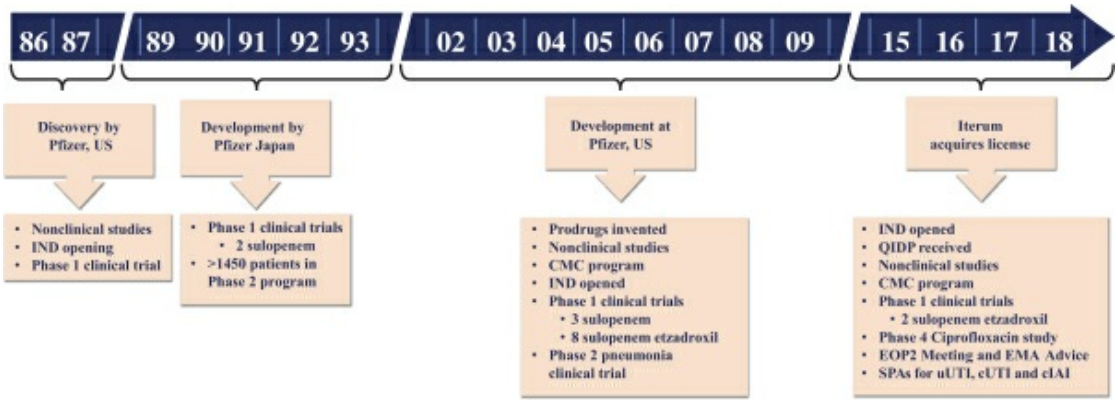
Given the growing prevalence of bacterial resistance that has rendered existing oral therapies ineffective, coupled with the FDA mandating new safety labeling changes to enhance warnings limiting fluoroquinolone use in uncomplicated infections due to the association with disabling and potentially permanent 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



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 support 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. QIDP designation status for other indications, such as respiratory tract infections, gonorrhea and diabetic foot infection, 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. We expect top-line delivery of data and submission of the program for regulatory review to the FDA in the second half of 2019.

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} ³ 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 ³ 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 planned 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
EBSL 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	³64	23	³64	0
Fosfomycin	8	98	128	86	64	95
Ciprofloxacin	³2	77	1	91	³2	74
Trimethoprim-Sulfamethoxazole	³32	74	³32	86	³32	58
Amoxicillin-Clavulanate	16	76	³16	80	³16	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.

Nonclinical 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
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
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(1)	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
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
		Total	395	

(1) Final report pending.

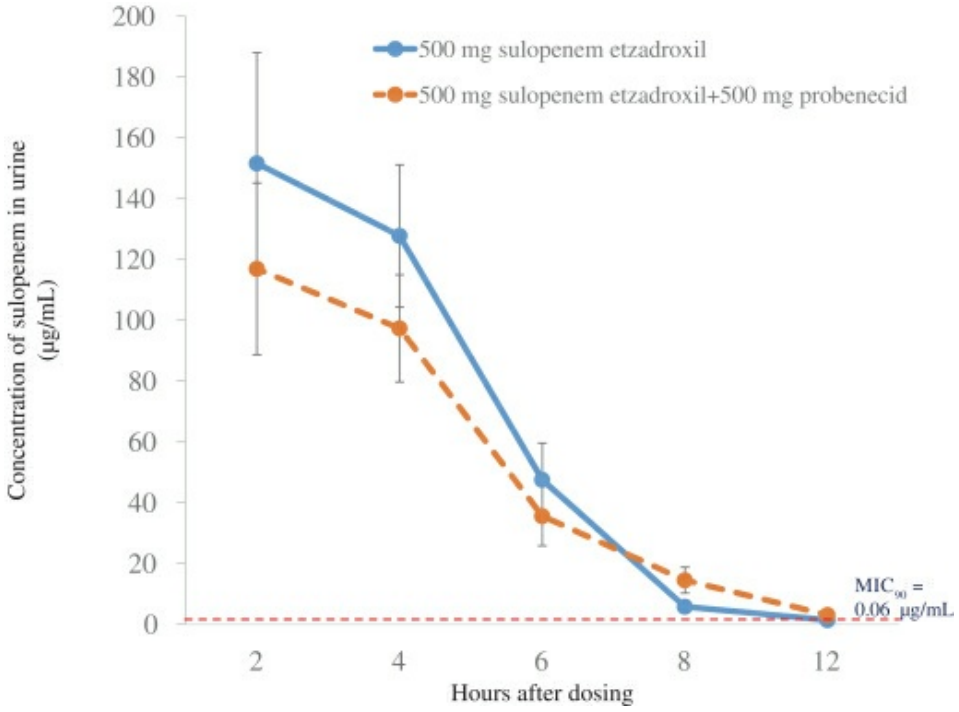
Oral Sulopenem

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 two Phase 1 clinical trials, IT001-101 and IT001-102, 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 C_{max} (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 co-administered with 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**	**C_{max} (ng/mL)**	**$AUC_{0-\infty}$ (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; C_{max} = maximum plasma concentration; $AUC_{0-\infty}$ = 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.

We plan to conduct additional Phase 1 clinical trials, including drug interaction studies with itraconazole and valproic acid and standard bioavailability and bioequivalency studies of new formulations, 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 (C_{max}). A representative analysis of pharmacokinetic parameters, a subset of study A1091001, is described in the table below.

	N	Dose (mg)	Infusion duration (h)	C_{max} (µg/mL)	AUC $_{0-\infty}$ (µg hr/mL)	$T_{1/2}$ (h)	CL_{total} (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; $T_{1/2}$ = half-life; CL_{total} = clearance (only measured on Day 14)

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 will be 1000 mg sulopenem delivered over 3 hours once a day. The oral dose will be 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 including skin 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 ³ 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 complicated intra-abdominal infections 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 symptoms, pyuria and bacteriuria.

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)

Threepatients 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 proposed 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 symptoms, pyuria and bacteriuria.

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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)	

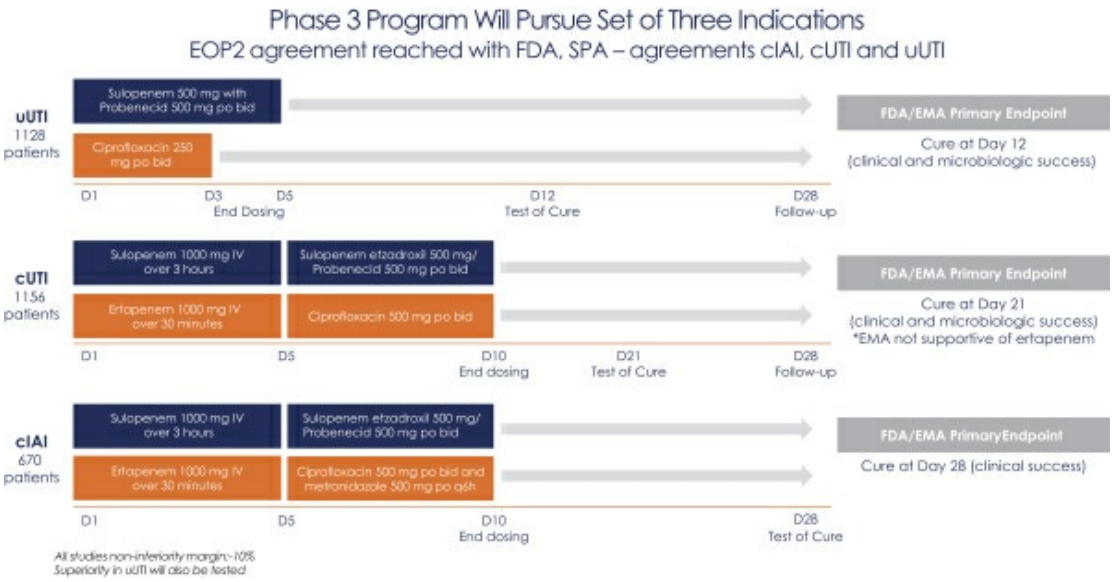
Phase 2 Clinical Trial with sulopenem and sulopenem etzadroxil

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.

Planned 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. Oral sulopenem alone will be studied for the treatment of outpatients with uUTI, while oral sulopenem and sulopenem will be studied for the treatment of cUTI and 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 will also test 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 is underway 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 will receive five days of sulopenem IV or comparator and then step down to two to five additional days of oral treatment with either oral sulopenem or ciprofloxacin. In the cIAI trial, clinical outcome at the test of cure visit will be 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. 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.

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



Safety 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 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)
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.

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 patents 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 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 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 in each 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 and 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 are obligated to pay Pfizer potential future clinical and 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 at a value of $15.71 per share as additional payment for the licensed rights. In addition, if we sublicense or assign our rights to 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. 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 own any patents or patent applications 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.

Licensed Intellectual Property Relating to Oral Sulopenem

As noted above, we have been granted an exclusive license from Pfizer under one patent in the United States and one patent each in Japan, Mexico and Hong Kong directed to the composition of matter, formulation and/or use of oral sulopenem. Our sulopenem program contains one United States patent covering composition of matter of sulopenem etzadroxil licensed exclusively to us. This United States patent is scheduled to expire in 2029, subject to potential extension under the Hatch-Waxman Act to 2034. The FDA has designated sulopenem and oral sulopenem as QIDPs for the indications of uUTI, cUTI and cIAI. QIDP status provides the potential for a more rapid new drug application (NDA) review cycle and adds five years to any other regulatory exclusivity period awarded. QIDP status for other indications, such as respiratory tract infections, gonorrhea and diabetic foot infection 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.

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 would compete with several oral antibiotics currently in clinical development, including ceftibuten clavulanate from Achaogen, Inc., tebipenem pivoxil from Spero Therapeutics, Inc., delafloxacin from Melinta Therapeutics, Inc, and omadacycline from Paratek Pharmaceuticals, Inc.

We also expect that oral sulopenem, if approved, would compete with future and current generic versions of marketed oral antibiotics. 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;
- a favorable safety and tolerability profile;
- a convenient oral dosing regimen and opportunity to step down from IV-administered therapy; and
- 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, Zerbaxa from Merck & Co. and Vabomere from Melinta Therapeutics, Inc. There are also a number of IV-administered product candidates in late-stage clinical development that are intended to treat gram-negative infections, including plazomicin from Achaogen Inc., cefiderocol from Shionogi & Co. Ltd. and imipenem-relabactam from Merck & Co.

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, 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. 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; and
- payment of user fees and securing FDA review and approval of the NDA.

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.

Clinical Trials

Clinical trials involve the administration of the IND 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 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.

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 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 risk evaluation and mitigation strategy (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 in order to secure final approval of 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. 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.

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, 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.

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.

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.

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.

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 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."

Some of the provisions of the ACA have yet to be implemented, and there have been legal and political challenges to certain aspects of the ACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018 (the BBA), among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Congress may consider other legislation to repeal or replace elements of the ACA.

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. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. 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 have increasingly passed legislation and implemented 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.

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 directly commercialize our sulopenem program in the United States 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. A team of regional medical physicians 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.

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 a 2017 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. We currently have a ten 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 sulopenem's active pharmaceutical ingredient at the time of submitting our NDAs, with each supplier capable of producing kilogram quantities for commercial scale 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.

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.

Facilities

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. We also lease office space in Old Saybrook, CT. 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.

Employees

As of March 31, 2018, we had 38 full-time employees, including a total of nine employees with M.D., Pharm.D. or Ph.D. degrees. Twenty-seven 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.

MANAGEMENT

Executive Officers and Directors

The following table sets forth certain information regarding our current executive officers and directors as of April 30, 2018:

Name	Age	Position(s)
Corey N. Fishman	53	President, Chief Executive Officer and Director
Michael W. Dunne, M.D.	58	Chief Scientific Officer
Judith M. Matthews	48	Chief Financial Officer
Jeff Schaffnit	47	Chief Commercial Officer
Paul R. Edick(1)(3)	62	Chairman of the Board of Directors
Brenton K. Ahrens(2)	55	Director
Mark Chin(1)(2)	36	Director
James I. Healy, M.D., Ph.D(1)	53	Director
Patrick J. Heron(3)	47	Director
Robert Hopfner, Ph.D	45	Director
Ronald M. Hunt(1)(3)	53	Director
David G. Kelly(2)(3)	57	Director
Shahzad Malik, M.D.(1)(3)	51	Director

(1) Member of the compensation committee.
(2) Member of the audit committee.
(3) Member of the nominating and corporate governance committee.

Executive Officers

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 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. 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.

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, 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. 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.

Jeff Schaffnit has served as our Chief Commercial Officer since February 2018. From April 2017 to January 2018, Mr. Schaffnit served as group vice president and head of patient engagement and experience at Shire plc, a biopharmaceutical company, where he previously served as vice president and head of U.S. hematology from June 2016 to March 2017. From January 2016 to June 2016, Mr. Schaffnit served as vice president and North American region head, hematology at Baxalta Inc., a biopharmaceutical company acquired by Shire. From January 2015 to December 2015, Mr. Schaffnit served as vice president of hemophilia marketing for Baxalta Inc. From August 2013 to December 2014, Mr. Schaffnit served as senior director, U.S. hemophilia marketing at Baxter International Inc., a healthcare company. From October 2012 to July 2013, Mr. Schaffnit served as vice president of sales and marketing at Mérieux NutriSciences Corporation, a food safety and nutrition consulting company. Mr. Schaffnit has a B.S. in chemical engineering from the University of Illinois at Urbana-Champaign and an M.B.A. in strategy, finance and marketing from the Kellogg School of Management at Northwestern University.

Non-Employee Directors

Paul R. Edick has served as Chairman of our board of directors since November 2015. Since January 2017, Mr. Edick has served as president, chief executive officer and a director of Xeris Pharmaceuticals, Inc., a biopharmaceutical company. Since November 2014, Mr. Edick served as founding partner of 3G Advisors, LLC, a consultancy to the pharmaceutical, healthcare and healthcare investor communities. From July 2010 to November 2014, Mr. Edick served as chief executive officer and member of the board of directors of Durata. From 2008 to 2010, Mr. Edick served as chief executive officer of GANIC Pharmaceuticals, Inc., a pharmaceutical company. From 2002 to 2008, Mr. Edick served in a variety of roles at MedPointe, including as chief executive officer from 2006 to 2008. Mr. Edick currently serves as a member of the board of directors of Newlink Genetics Corporation, Sucampo Pharmaceuticals, Inc., Neos Therapeutics, Inc., PDL BioPharma, Inc. and Xeris Pharmaceuticals. Mr. Edick previously served on the boards of directors of Circassia Pharmaceuticals and Durata. Mr. Edick holds a B.A. in psychology from Hamilton College in Clinton, New York. We believe Mr. Edick is qualified to serve on our board of directors due to his extensive experience with pharmaceutical companies at various stages of development, including service on the boards of directors of other healthcare companies.

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, Ethicon (J&J), and IAP Research. Mr. Ahrens previously served on the board of directors of Durata. 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 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.

James I. Healy, M.D., Ph.D. has served as a member of our board of directors since November 2015. Dr. Healy has been a general partner at Sofinnova Ventures, Inc. since 2000. Prior to this, Dr. Healy held positions at Bayer Healthcare Pharmaceuticals Inc. and Sanderling Ventures. Dr. Healy is currently on the board of directors of Ascendis Pharma A/S, Coherus BioSciences, Inc., Edge Therapeutics, Inc., ObsEva SA, Natera, Inc., NuCana plc and several private companies. Previously, Dr. Healy served as a board member of Amarin Corporation plc, Anthera Pharmaceuticals, Inc., Auris Medical Holding AG, Durata, Hyperion Therapeutics, Inc., InterMune, Inc., KaloBios Pharmaceuticals, Inc., Movetis NV and a number of private companies. Dr. Healy holds a B.A. in molecular biology and a B.A. in Scandinavian studies from the University of California at Berkeley and an M.D. and Ph.D. in immunology from Stanford University School of Medicine. We believe Dr. Healy is qualified to serve on our board of directors due to his medical training and his extensive experience in the biopharmaceutical industry, including as a venture capital investor and a member of the boards of directors of other biopharmaceutical companies.

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 Tobira Therapeutics, Inc. and Collegium 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.

Robert Hopfner, Ph.D. has served as a member of our board of directors since December 2017. Since October 2017, Dr. Hopfner has served as a managing partner at Pivotal bioVenture Partners LLC, a venture capital firm. From 2007 to September 2017, Dr. Hopfner served as an investment partner at Bay City Capital, a venture capital firm. Before joining Bay City Capital, Dr. Hopfner worked as an associate in DuPont Pharmaceuticals' business development & strategic planning group and as an analyst at Ag-West Biotech, a Western Canadian seed-stage biotech venture capital firm. Dr. Hopfner previously served on the boards of directors of Durata and Hyperion Therapeutics, Inc. Dr. Hopfner holds Ph.D. in pharmacology and a B.S. in pharmacy from the University of Saskatchewan and an M.B.A. with specializations in entrepreneurship, finance and strategy from the University of Chicago Booth School of Business. We believe Dr. Hopfner is qualified to serve on our board of directors due to his investment experience in the life science industry, as well as his medical background.

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 previously served on the board of directors of Durata and Relypsa, 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. Since September 2014, Mr. Kelly has served as the executive vice president, managing director, Ireland of Horizon Pharma, plc, a biopharmaceutical company. 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 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 also currently serves on the board of directors of Versartis, Inc. He previously served on the boards of directors of Conatus Pharmaceuticals Inc. and Agenus Inc. 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.

Family Relationships

There are no family relationships among any of the directors or executive officers.

Board Composition

Our business and affairs are managed under the direction of our board of directors, which currently consists of ten members. Certain members of our board of directors were elected pursuant to the provisions of a voting agreement among certain of our shareholders. Under the terms of this voting agreement, the shareholders who are party to the voting agreement have agreed to vote their respective shares so as to elect directors as follows: (i) one individual designated by Frazier Healthcare VII, L.P. and Frazier Healthcare VII-A, L.P. (Mr. Heron), (ii) one individual designated by Canaan X, L.P. (Mr. Ahrens), (iii) one individual designated by New Leaf Ventures III, L.P. (Mr. Hunt), (iv) one individual designated by Sofinnova Venture Partners IX, L.P. (Dr. Healy), (v) one individual designated by Arix Bioscience Holdings Ltd. (Mr. Chin), (vi) one individual designated by Pivotal bioVenture Partners I, L.P. (Dr. Hopfner), (vii) one individual designated by Advent Life Sciences LLP and Advent Life Sciences Fund II LP (Dr. Malik), (viii) the person then serving as Chief Executive Officer (Mr. Fishman), (ix) a Chairman of the Board acceptable to at least a majority of the board of directors (Mr. Edick) and (x) one industry representative not affiliated with our company or any investor in our company acceptable to at least a majority of the board of directors (Mr. Kelly). The voting agreement will terminate upon the completion of this offering and none of our shareholders will have any special rights regarding the election or designation of members of our board of directors.

Contingent upon and immediately prior to the effectiveness of the registration statement of which this prospectus forms a part, Dr. Hopfner will resign from our board of directors, and on completion of this offering, we will reduce our authorized number of directors to nine. Upon completion of this offering, our directors will be divided among three classes with staggered three-year terms as follows:

- Class I, whose members will be Mark Chin, Paul Edick and David G. Kelly. The terms of the Class I directors will expire at our 2019 annual meeting of shareholders;
- Class II, whose members will be Patrick J. Heron, Shahzad Malik, M.D. and Brenton K. Ahrens. The terms of the Class II directors will expire at our 2020 annual meeting of shareholders; and
- Class III, whose members will be Corey Fishman, James I. Healy, Ph.D., M.D. and Ronald M. Hunt. The terms of the Class III directors will expire at our 2021 annual meeting of shareholders.

We have applied to list our ordinary shares on the Nasdaq Global Market, or Nasdaq. Applicable Nasdaq rules 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, (i) on the date of the completion of the offering, at least one member of each of a listed company's audit, compensation and nominating and corporate governance

committees be independent, (ii) within 90 days of the date of the completion of the offering, a majority of the members of such committees be independent and (iii) within one year of the date of the completion of the offering, all the members of such committees be independent. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 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.

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 all directors other than Corey Fishman are "independent directors" as defined under applicable Nasdaq rules. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company 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 capital stock by each non-employee director.

Committees of the Board of Directors

Our board of directors has the authority to appoint committees to perform certain management and administration functions. Our board of directors has established an audit committee, a compensation committee, and a nominating and corporate governance committee. The composition and responsibilities of each committee are described below. Members will serve on these committees until their resignation or until otherwise determined by the board of directors. Following the closing of this offering, the charters for each of these committees will be available on our website at www.iterumtx.com. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only. The composition of all of our committees will comply with all applicable requirements of the Irish Companies Act, the Sarbanes-Oxley Act of 2002, Nasdaq and Securities and Exchange Commission (SEC), rules and regulations.

Audit Committee

Upon the completion of this offering, our audit committee will consist of Brenton K. Ahrens, Mark Chin and David G. Kelly. Our board of directors has determined each of Mr. Ahrens, Mr. Chin and Mr. Kelly to be independent under the listing standards and Rule 10A-3(b)(1) of the Exchange Act and for the purposes of Section 167(4) of the Irish Companies Act. The chairperson of our audit committee is Mr. Kelly. 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 Nasdaq. 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.

The primary purpose of the audit committee is to discharge the responsibilities of our board of directors with respect to our accounting, financial, and other reporting and internal control practices and to oversee our independent registered accounting firm. Specific responsibilities of our audit committee include:

- recommending a qualified firm to serve as the independent registered public accounting firm to audit our financial statements to the board of directors;

- helping to ensure the independence and performance of the independent registered public accounting firm;
- discussing the scope and results of the audit with the independent registered public accounting firm, and reviewing, with management and the independent accountants, our interim and year-end operating results;
- reviewing, upon completion of the audit, the Irish statutory financial statements proposed to be filed with our annual return at the Irish Companies Registration Office;
- developing procedures for employees to submit concerns anonymously about questionable accounting or audit matters;
- reviewing our policies on risk assessment and risk management;
- reviewing related party transactions;
- coordinating the board of directors' oversight of our internal controls over financial reporting, including discussing with management and the independent registered public accounting firm the integrity of our financial reporting processes and internal controls; and
- approving (or, as permitted, pre-approving) all audit and all permissible non-audit services to be performed by the independent registered public accounting firm.

Compensation Committee

Our compensation committee consists of Paul R. Edick, Mark Chin, James I. Healy, M.D., Ph.D., Ronald M. Hunt and Shahzad Malik, M.D. Our board of directors has determined each of Mr. Edick, Mr. Chin, Dr. Healy, Mr. Hunt and Dr. Malik to be a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act. The chairperson of our compensation committee is Mr. Hunt.

The primary purpose of our compensation committee is to discharge the responsibilities of our board of directors to oversee our compensation policies, plans and programs and to review and determine the compensation to be paid to our executive officers, directors and other senior management, as appropriate. Specific responsibilities of our compensation committee include:

- reviewing and approving, or recommending that our board of directors approve, the compensation of our executive officers;
- reviewing and recommending to our board of directors the compensation of our directors;
- reviewing and approving, or recommending that our board of directors approve, the terms of compensatory arrangements with our executive officers;
- administering our stock and equity incentive plans;
- selecting independent compensation consultants, legal counsel or other advisors;
- reviewing and approving, or recommending that our board of directors approve, incentive compensation and equity plans, severance agreements, change-of-control protections and any other compensatory arrangements for our executive officers; and
- reviewing and making recommendations to our board of directors regarding incentive compensation and equity plans.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Paul R. Edick, Patrick J. Heron, Ronald M. Hunt, David G. Kelly and Shahzad Malik, M.D. Our board of directors has determined each of Mr. Edick, Mr. Heron, Mr. Hunt, Mr. Kelly and Dr. Malik to be independent under the listing standards. The chairperson of our nominating and corporate governance committee is Mr. Edick.

Specific responsibilities of our nominating and corporate governance committee include:

- reviewing periodically and evaluating director performance on our board of directors and its applicable committees, and recommending to our board of directors and management areas for improvement;
- interviewing, evaluating, nominating and recommending individuals for membership on our board of directors;
- administering the process outlined in our constitution concerning shareholder nominations for director candidates;
- reviewing developments in corporate governance practices;
- overseeing and reviewing our processes and procedures to provide information to our board of directors and its committees;
- overseeing succession planning for senior executives;
- reviewing and recommending to our board of directors any amendments to our corporate governance policies; and
- reviewing and assessing, at least annually, the performance of the nominating and corporate governance committee and the adequacy of its charter.

Code of Business Conduct and Ethics

We will adopt a Code of Business Conduct and Ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. Following the closing of this offering, the Code of Business Conduct and Ethics will be available on our website at www.iterumtx.com. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only. We intend to disclose any amendments to the Code of Business Conduct and Ethics, or any waivers of its requirements, on our website to the extent required by the applicable rules and exchange requirements.

Compensation Committee Interlocks and Insider Participation

No member of our compensation committee 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.

2017 Non-Employee Director Compensation

The following table sets forth information regarding compensation earned by or paid to our non-employee directors during 2017.

Name	Fees Earned or Paid in Cash	Option Awards(1)	Other Compensation	Total
Brenton K. Ahrens	$ —	$ —	$ —	$ —
Mark Chin	—	—	—	—
Paul R. Edick(2)	30,000	1,992(2)	—	31,992
James I. Healy	—	—	—	—
Patrick J. Heron	—	—	—	—
Robert Hopfner, Ph.D	—	—	—	—
Ronald M. Hunt	—	—	—	—
David G. Kelly(3)(4)	25,000	1,195(3)	—	26,195
Shahzad Malik, M.D.	—	—	—	—

(1) The amounts reported do not reflect the amounts actually received by our non-employee directors. Instead, these amounts reflect the aggregate grant date fair value of each stock option granted to our non-employee directors during 2017, 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 9 to our audited financial statements included in this prospectus. As required by SEC rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions. Our non-employee 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. The table below lists the aggregate number of shares subject to outstanding option awards held by each of our non-employee directors.

Name	Number of Shares Subject to Outstanding Options as of December 31, 2017
Brenton K. Ahrens	—
Mark Chin	—
Paul R. Edick(2)	1,060
James I. Healy	—
Patrick J. Heron	—
Robert Hopfner, Ph.D	—
Ronald M. Hunt	—
David G. Kelly(3)	3,182
Shahzad Malik, M.D.	—

(2) Mr. Edick was granted an option to purchase 1,060 of our ordinary shares at an exercise price of $3.30 per share on September 12, 2017. The shares are scheduled to vest over a four-year period as follows: 1/4th of the shares vest on the one-year anniversary of the vesting commencement date, September 12, 2017, and 1/48th of the total shares will vest each month thereafter, subject to continued service with us through each relevant vesting date. The vesting of Mr. Edick's option award will accelerate in full if within 30 days prior to or 12 months following a change of control Mr. Edick (i) is terminated without cause or (ii) resigns for good reason.

(3) Mr. Kelly was granted an option to purchase 636 of our ordinary shares at an exercise price of $3.30 per share on September 12, 2017. The shares are scheduled to vest over a four-year period as follows: 1/4th of the shares vest on the one-year anniversary of the vesting commencement date, September 12, 2017, and 1/48th of the total shares will vest each month thereafter, subject to continued service with us through each relevant vesting date. The vesting of Mr. Kelly's option award will accelerate in full if within 30 days prior to or 12 months following a change of control Mr. Kelly (i) is terminated without cause or (ii) resigns for good reason.

(4) Mr. Kelly receives $20,000 per annum for his service as a director of Iterum Therapeutics plc, and $5,000 for his service as a director of our Irish subsidiary, Iterum Therapeutics International Limited. Mr. Kelly's compensation is set in US$, however he is paid in Euros using the average exchange rate for the 12 months ended December 31, 2016. Applying this formula to the year ended December 31, 2017, US$1.00 was equal to €0.9034.

Non-Employee Director Compensation Policy

In May 2018, our board of directors adopted a non-employee director compensation policy effective upon execution of the underwriting agreement for this offering, pursuant to which our non-employee directors are compensated with an annual cash retainer. Each such 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 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 stock option to be granted under this policy will be determined using the same method we use to calculate the grant-date fair value of stock 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).

EXECUTIVE COMPENSATION

Our named executive officers, consisting of our principal executive officer and the next two most highly compensated executive officers, as of December 31, 2017, were:

- Corey N. Fishman, President and Chief Executive Officer;
- Michael W. Dunne, M.D., Chief Scientific Officer; and
- Judith M. Matthews, Chief Financial Officer.

2017 Summary Compensation Table

The following table presents all of the compensation paid or awarded to or earned by our named executive officers during 2017:

Name and Principal Position	Year	Salary	Option Awards(1)	Non-Equity Incentive Plan Compensation(2)	All Other Compensation(3)	Total
Corey N. Fishman *President and Chief Executive Officer*	2017	$420,000	$122,694	$ 210,000	$ 2,208	$754,902
Michael W. Dunne, M.D. *Chief Scientific Officer*	2017	367,500	78,078	154,350	3,741	603,669
Judith M. Matthews *Chief Financial Officer*	2017	236,250	22,038	59,063	788	318,139

(1) The amounts reported do not reflect the amounts actually received by our executive officers. Instead, these amounts reflect the aggregate grant date fair value of each stock option granted to our executive officers during 2017, 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 9 to our audited financial statements included in this prospectus. 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 period from January 1, 2017 to December 31, 2017, and exclude payments made in 2017 for 2016 bonuses.

(3) Includes the dollar value of life insurance premiums paid by the company for the benefit of such executive.

Outstanding Equity Awards as of December 31, 2017

The following table presents information regarding outstanding equity awards held by our named executive officers as of December 31, 2017. All stock options were granted under our 2015 Equity Incentive Plan.

			Option Awards			
Name	Grant Date	Vesting Commencement Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable(1)(2)	Option Exercise Price Per Share(3)	Option Expiration Date
Corey N. Fishman	09/12/2017	09/12/2017	—	65,351	$ 3.30	09/11/2027
Michael W. Dunne, M.D.	09/12/2017	09/12/2017	—	41,587	3.30	09/11/2027
Judith M. Matthews	09/12/2017	09/12/2017	—	11,882	3.30	09/11/2027

(1) The shares are scheduled to vest over a four-year period as follows: 1/4 th of the shares underlying the options vest on the one-year anniversary of the vesting commencement date and thereafter 1/48th of the total shares vest each month, subject to continued service with us through each relevant vesting date.

(2) Pursuant to the equity agreements between the named executive officer and us, the vesting of such named executive officer's stock and option awards will accelerate under certain circumstances as described under the section titled "—Employment, Severance and Change in Control Arrangements."
(3) The exercise price per share of the stock options reflects the fair market value per ordinary share on the date of grant.

Pension Benefits

Our named executive officers did not participate in, or otherwise receive any benefits under, any pension or defined benefit retirement plan sponsored by us in 2017.

Nonqualified Deferred Compensation

Our named executive officers did not participate in, or earn any benefits under, a non-qualified deferred compensation plan sponsored by us during 2017.

Emerging Growth Company Status

We are an "emerging growth company," as defined in the JOBS Act. As an emerging growth company we will be exempt from certain requirements related to executive compensation, including, but not limited to, the Nasdaq requirements to hold a nonbinding advisory vote on executive compensation and to provide information relating to the ratio of total compensation of our Chief Executive Officer to the median of the annual total compensation of all of our employees, each as required by the Investor Protection and Securities Reform Act of 2010, which is part of the Dodd-Frank Wall Street Reform and Consumer Protection Act.

Employment, Severance and Change in Control Arrangements

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 of proprietary information agreement. Any potential payments and benefits due upon a termination of employment or a change of control of us are further described below.

Corey N. Fishman

Mr. 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. Effective upon the closing of this offering, Mr. Fishman's base salary will be $540,000, and his discretionary annual target performance bonus will be 55% of his annual base salary. In connection with his employment, in September 2017 Mr. Fishman was granted an option to purchase 65,351 of our ordinary shares at an exercise price of $3.30 per share. The shares underlying the option vest as to 1/4th on the one-year anniversary of the vesting commencement date and 1/48th of the total shares vest each month thereafter, subject to Mr. Fishman's continued service with us through each relevant vesting date. The vesting of Mr. Fishman's option award is also subject to acceleration as detailed in the section titled "—Potential Payments Upon Termination or Change in Control."

Michael W. Dunne, M.D.

Dr. Dunne 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 current base salary is $367,500, and his discretionary annual target performance bonus is 40% of his annual base salary. In connection with his employment, in September 2017 Dr. Dunne was granted an option to purchase 41,587 of our ordinary shares at

an exercise price of $3.30 per share. The shares underlying the option vest as to 1/4th on the one-year anniversary of the vesting commencement date and 1/48th of the total shares vest each month thereafter, subject to Dr. Dunne's continued service with us through each relevant vesting date. The vesting of Dr. Dunne's option award is also subject to acceleration as detailed in the section titled "—Potential Payments Upon Termination or Change in Control."

Judith M. Matthews

Ms. 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. Effective upon the closing of this offering, Ms. Matthews' base salary will be $350,000, and her discretionary annual target performance bonus will be 35% of her annual base salary. In connection with her employment, in September 2017 Ms. Matthews was granted an option to purchase 11,882 of our ordinary shares at an exercise price of $3.30 per share. The shares underlying the option vest as to 1/4th on the one-year anniversary of the vesting commencement date and 1/48th of the total shares vest each month thereafter, subject to Ms. Matthews' continued service with us through each relevant vesting date. The vesting of Ms. Matthews' option award option award is also subject to acceleration as detailed in the section titled "—Potential Payments Upon Termination or Change in Control."

Potential Payments Upon Termination or Change in Control

Our offer letter 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, effective upon the closing of this offering, be entitled to receive the following severance benefits:

- cash severance equal to a fixed number of months of such executive's base salary (effective upon the closing of this offering, 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 stock options 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.

In addition, pursuant to ordinary share subscription deeds dated as of October 14, 2015, upon a change in control each of Mr. Fishman, Dr. Dunne and Ms. Matthews are entitled to acceleration of all of the remaining unvested ordinary shares issued thereunder, provided that such individual remains a service provider as of the time of consummation of the change in control.

Equity Incentive Plans

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 employees, consultants, and directors with the financial interests of our shareholders. In addition, we believe that our ability to grant options and other equity-based awards helps us to attract, retain, and motivate employees, consultants, and directors and encourages them to devote their best efforts to our business and financial success. The principal features of our equity incentive plans are summarized below. These summaries are qualified in their entirety by reference to the actual text of the plans, which are filed as exhibits to the registration statement of which this prospectus is a part.

2018 Equity Incentive Plan

Our board of directors adopted the 2018 Equity Incentive Plan, or the 2018 Plan, in March 2018 and our shareholders approved the 2018 Plan in May 2018. The 2018 Plan will become effective immediately on the execution and delivery of the underwriting agreement related to this offering. Once the 2018 Plan is effective, no further grants will be made under the 2015 Equity Incentive Plan, or the 2015 Plan.

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. We may grant ISOs to our employees and employees of a subsidiary corporation or parent corporation (within the meaning of Sections 424(e) and 424(f) of the Code).

Share Reserve. Initially, the aggregate number of our ordinary shares that may be issued pursuant to awards under our 2018 Plan is 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 (assuming the 2018 Plan becomes effective in calendar year 2018) 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. 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 will be administered by our compensation committee, or by our board of directors or another duly authorized committee or by 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 stock awards, and determine the number of shares subject to such stock awards.

Our compensation committee will have 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 to or repurchased by us.

Restricted Stock Unit Awards. RSUs 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 award has not been forfeited, then on the date specified in the RSU 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 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 Companies Act 2014 of the Republic of Ireland or (z) Chapter 2 of Part 9 of the Companies Act 2014 of the Republic of Ireland.

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 stockholders. 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 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.

Upon the effectiveness of the 2018 Plan, we will no longer grant awards under the 2015 Plan. However, any outstanding awards granted under the 2015 Plan will 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 March 31, 2018, we have reserved 443,029 ordinary shares for issuance under our 2015 Plan. As of March 31, 2018, options to purchase 248,128 ordinary shares were outstanding under our 2015 Plan, with a weighted-average exercise price of $3.31 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 is administered by our board of directors or another duly authorized committee. Following the offering, our 2015 Plan will be 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 the substantially the same 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 stockholders.

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. For a description of these protections, see the section titled "Description of Share Capital —Indemnification of Directors and Officers; Insurance."

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 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 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. Prior to 180 days after the date of this offering, the sale of any shares under such plan would be subject to the lock-up agreement that the director or officer has entered into with the underwriters.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a summary of transactions since January 1, 2015 to which we have been a participant, in which:

- the amount involved exceeded or will exceed $120,000; and
- any of our directors, executive officers, or holders of more than 5% of our ordinary shares, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest, other than compensation and other arrangements that are described in the section titled "Executive Compensation" or that were approved by our compensation committee.

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 in arm's-length transactions.

Sales of Preferred Shares

In November 2015, we issued an aggregate of 1,514,320 of our Series A preferred shares at a purchase price of $15.71 per share for an aggregate cash purchase price of $20.7 million plus the receipt of intellectual property pursuant to our license agreement with Pfizer. In December 2016, we issued an aggregate of 1,518,137 of our Series A preferred shares at a purchase price of $15.71 per share for an aggregate cash purchase price $20.9 million plus the receipt of intellectual property pursuant to our license agreement with Pfizer. In May 2017, we issued an aggregate of 2,654,206 of our Series B-1 preferred shares at a purchase price of $17.28 per share for an aggregate purchase price $45.9 million. In February 2018, we issued an aggregate of 1,709,650 of our Series B-2 preferred shares at a purchase price of $18.85 per share for an aggregate purchase price of $32.2 million. The following table summarizes purchases of preferred shares by holders of more than 5% of our capital shares and their affiliated entities, our directors and our executive officers.

Name	Series A Preferred Shares	Series B-1 Preferred Shares	Series B-2 Preferred Shares	Aggregate Purchase Price
Entities affiliated with Advent Life Sciences(1)	—	405,068	226,109	$ 11,262,624
Arix Bioscience Holdings Ltd.(2)	—	445,576	248,721	12,388,888
Canaan X, L.P.(3)	721,408	275,446	229,660	20,422,894
Entities affiliated with Frazier Healthcare(4)	636,536	243,040	202,641	18,020,199
New Leaf Ventures III, L.P.(5)	466,793	178,230	148,603	13,214,813
Pivotal bioVenture Partners Fund I, L.P.(6)	—	405,069	226,109	11,262,625
Sofinnova Venture Partners IX, L.P.(7)	721,408	275,446	229,660	20,422,894
Corey N. Fishman	33,259	4,050	1,591	622,500
Michael W. Dunne, M.D.	12,730	4,050	2,917	324,999
Judith M. Matthews	10,980	3,038	2,466	271,500
Paul R. Edick	15,913	4,050	1,591	350,000
David G. Kelly	9,548	—	—	150,000

(1) Includes preferred shares purchased by Advent Life Sciences LLP and Advent Life Sciences Fund II LP. Dr. Malik, a member of our board of directors, is a general partner of Advent Life Sciences.
(2) Mr. Chin, a member of our board of directors, is an investment director of Arix Bioscience.
(3) Mr. Ahrens, a member of our board of directors, is a general partner of Canaan.
(4) Includes preferred shares purchased by Frazier Healthcare VII, L.P. and Frazier Healthcare VII-A, L.P. Mr. Heron, a member of our board of directors, is a general partner of Frazier Healthcare Partners.
(5) Mr. Hunt, a member of our board of directors, is a managing director of New Leaf Ventures Partners.
(6) Dr. Hopfner, a member of our board of directors, is a managing partner of Pivotal bioVenture Partners.
(7) Dr. Healy, a member of our board of directors, is a general partner of Sofinnova Ventures.

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 capital stock, our executive officers, certain of our directors, and entities affiliated with certain of our directors. After the closing of this offering, these holders will be 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. For a more detailed description of these registration rights, see the section titled "Description of Share Capital—Registration Rights." In addition, this agreement gives 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 will terminate by its terms upon the completion of our initial public offering.

Offer Letters

We have entered into offer letters with our executive officers. For more information regarding these offer letters, see the section titled "Executive Compensation—Employment, Severance and Change in Control Arrangements."

Equity Grants

We have granted stock options to certain non-employee members of our board of directors. For a description of these stock options, see the section titled "Management—2017 Non-Employee Director Compensation."

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.

Related Party Transaction Policy

We will adopt a formal written policy in connection with this offering 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, will be 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.

All of the transactions described in this section were entered into prior to the adoption of this policy. Although we have not had a written policy for the review and approval of transactions with related persons, our board of directors has historically reviewed and approved any transaction where a director or officer had a financial interest, including the 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.

PRINCIPAL SHAREHOLDERS

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of April 30, 2018 by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our ordinary shares;
- each of our named executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

The percentage of shares beneficially owned before the offering shown in the table is based on 7,809,423 ordinary shares outstanding as of April 30, 2018, after giving effect to the conversion of all of our Series A preferred shares, Series B-1 preferred shares and Series B-2 preferred shares into ordinary shares. The percentage of shares beneficially owned after this offering assumes the sale by us of 5,333,333 ordinary shares in this offering.

Certain of our directors and existing shareholders, or their affiliates, have indicated an interest in purchasing up to an aggregate of approximately $35.0 million of our ordinary shares in this offering. However, since such purchases have been neither confirmed nor allocated, any amounts that may be purchased by these existing shareholders in this offering have not been included in the following table.

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 stock options that are exercisable within 60 days of April 30, 2018. Our ordinary shares issuable pursuant to stock 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.

Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o Iterum Therapeutics plc, 200 South Wacker Dr., Suite 650, Chicago, IL 60606.

Name of Beneficial Owner	Shares Beneficially Owned Prior to Offering		Shares Beneficially Owned After the Offering	
	Number	Percent	Number	Percent
Greater than 5% shareholders:				
Entities affiliated with Advent Life Sciences(1)	631,177	8.1%	631,177	4.8%
Arix Bioscience Holdings Ltd.(2)	694,297	8.9	694,297	5.3
Canaan X, L.P.(3)	1,226,514	15.7	1,226,514	9.3
Entities affiliated with Frazier Healthcare(4)	1,082,217	13.9	1,082,217	8.2
New Leaf Ventures III, L.P.(5)	793,626	10.2	793,626	6.0
Pivotal bioVenture Partners Fund I, L.P.(6)	631,178	8.1	631,178	4.8
Sofinnova Venture Partners IX, L.P.(7)	1,226,514	15.7	1,226,514	9.3
Directors and Named Executive Officers:				
Corey N. Fishman	234,953	3.0	234,953	1.8
Michael Dunne, MD	144,458	1.8	144,458	1.1
Judith M. Matthews	52,130	*	52,130	*
Brenton K. Ahrens(3)	1,226,514	15.7	1,226,514	9.3
Mark Chin(2)	694,297	8.9	694,297	5.3
Paul R. Edick	24,736	*	24,736	*
James I. Healy, M.D., Ph.D(7)	1,226,514	15.7	1,226,514	9.3
Patrick J. Heron(4)	1,082,217	13.9	1,082,217	8.2
Robert Hopfner, Ph.D(6)	631,178	8.1	631,178	4.8
Ronald M. Hunt(5)	793,626	10.2	793,626	6.0
David G. Kelly(8)	10,714	*	10,714	*
Shahzad Malik, M.D.(1)	631,177	8.1	631,177	4.8
All current executive officers and directors as a group(9)	6,752,514	86.5	6,752,514	51.4

(1) Consists of (a) 21,692 shares held by Advent Life Sciences LLP and (b) 609,485 shares held by Advent Life Sciences Fund II LP. 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 these entities is 158-160 North Gower Street, London, NW1 2ND England.

(2) The shares are held directly by Arix Bioscience Holdings Ltd. Mr. Chin, a member of our board of directors, is an investment director of Arix Bioscience Holdings Ltd. The address for Arix Bioscience Holdings Ltd. is 20 Berkeley Square, Mayfair, London W1J 6EQ, United Kingdom.

(3) The shares are held directly by Canaan X L.P. Canaan Partners X LLC is the general partner of Canaan X L.P. and may be deemed to have sole investment and voting power over the shares held by Canaan X L.P. Mr. Ahrens, a member of our board of directors, Stephen M. Bloch, Daniel T. Ciporin, Wende S. Hutton, Maha S. Ibrahim, Deepak Kamra, Nina Kjellson, Guy M. Russo, Tim 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 Canaa Partners X LLC, collectively. The address for Canaan X L.P. is 2765 Sand Hill Road, Menlo Park, CA 94025.

(4) Consists of (a) 842,212 shares held directly by Frazier Healthcare VII, L.P. and (b) 240,005 shares held directly by Frazier Healthcare VII-A, L.P. 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. The general partner of FHM VII, L.P. is FHM VII, L.L.C., a Delaware limited liability company. Dr. 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 these entities is 601 Union Street, Suite 3200, Seattle WA 98101.

(5) Represents shares directly beneficially owned by New Leaf Ventures III, L.P. (“NLV-III”). New Leaf Venture Associates III, L.P. (“NLVA-III LP”) is the general partner of NLV-III and New Leaf Venture Management III, L.L.C. (“NLVM-III LLC”) is the general partner of NLVA-III LP. Mr. Hunt, a member of our board of directors, Vijay K. Lathi, and Liam Ratcliffe are individual managers of NLVM-III LLC. The address for this stockholder is Times Square Tower, 7 Times Square, Suite 3502, New York, NY 10036.

(6) 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. Richard Coles, Peter Bisgaard and Vincent Sai Sing Cheung are directors of Pivotal bioVenture Partners Fund I U.G.P., Ltd and may, along with Pivotal bioVenture Partners Fund I U.G.P., Ltd, be deemed to have shared voting and dispositive power over the shares owned by Pivotal bioVenture Partners Fund I, L.P. The registered office for these entities is Cricket Square, Hutchins Drive, PO Box 2681, George Town, Grand Cayman, KY1-1111. The address for these entities is 1700 Owners Street, Suite 595, San Francisco, CA 94158.

(7) The shares are held directly by Sofinnova Venture Partners IX, L.P. (“SVP IX”). Sofinnova Management IX, L.L.C. (“SM IX”) is the general partner of SVP IX. Each of Dr. Healy, a member of our board of directors, Anand Mehra and Michael Powell is a managing member of SM IX and may, along with SM IX, be deemed to have shared voting and dispositive power over the shares owned by SVP IX. The address for these entities is 3000 Sand Hill Road, Bldg. 4, Suite 250, Menlo Park, CA 94025.

(8) Consists of (a) 9,548 shares held directly and (b) 1,166 shares issuable pursuant to stock options exercisable within 60 days of April 30, 2018.
(9) Consists of (a) 6,751,348 shares held by the current directors and executive officers and (b) 1,166 shares issuable pursuant to stock options exercisable within 60 days of April 30, 2018.

DESCRIPTION OF SHARE CAPITAL

The following is a summary of some of the terms of our ordinary shares, based on our Articles of Association, as they will become effective upon their amendment prior to the completion of this offering, and the Irish Companies Act.

The following summary is subject to, and is qualified in its entirety by reference to, the provisions of our Articles of Association, the form of which is filed as an exhibit to the registration statement of which this prospectus is a part.

Except as otherwise specified below, references to voting by our shareholders contained in this Description of Share Capital are references to voting by holders of ordinary shares entitled to attend and vote generally at general meetings of our shareholders.

Organization

We are an Irish public limited company. We were incorporated in Ireland on June 24, 2015 under the name Iterum Therapeutics Limited with registered number 563531 and were re-registered as a public limited company in March 2018 under the name Iterum Therapeutics plc. Our affairs are governed by our Constitution including our Articles of Association that will come into effect immediately upon completion of this offering and Irish law.

Objective

As provided by and described in our Constitution, our principal objective is to carry on the business of a holding company and all associated related activities and to carry on various activities associated with that objective.

Share Capital

Immediately after the completion of this offering, our authorized share capital will be $1,500,000, divided into 50,000,000 ordinary shares with a nominal value of $0.01 per share and 100,000,000 undesignated preferred shares with a nominal value of $0.01 per share. Upon the completion of this offering and the use of proceeds therefrom, we expect to have 13,142,756 ordinary shares outstanding, including 146,309 ordinary shares issued pursuant to restricted stock issuances that are subject to repurchase, and no outstanding shares of any other class.

The rights and restrictions to which the ordinary shares will be subject will be prescribed in our Articles of Association. Our Articles of Association entitle the Board, without shareholder approval, to determine the terms of the undesignated preferred shares issued by us.

Irish law does not recognize fractional shares held of record. Accordingly, our Articles of Association will not provide for the issuance of fractional shares of Iterum, and the official Irish register of Iterum will not reflect any fractional shares.

Whenever an alteration or reorganization of the share capital of Iterum would result in any Iterum shareholder becoming entitled to fractions of a share, the Board of Iterum 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.

Transfer and Registration of Shares

Our share register will be maintained by our transfer agent. Registration in this share register will be determinative of membership in us. Any of our shareholders who only hold ordinary shares beneficially will not

be the holder of record of such ordinary shares. Instead, the depository or other nominee will be the holder of record of such shares. Accordingly, a transfer of ordinary shares from a person who holds such ordinary shares beneficially to a person who will also hold such ordinary shares beneficially through the same depository or other nominee will not be registered in our official share register, as the depository or other nominee will remain the holder of record of such ordinary shares.

A written instrument of transfer will be required under Irish law in order to register on our official share register any transfer of ordinary shares (i) from a person who holds such ordinary shares directly to any other person or (ii) from a person who holds such ordinary shares beneficially to another person who also will hold such ordinary shares beneficially where the transfer involves a change in the depository or other nominee that is the record owner of the transferred ordinary shares. An instrument of transfer will be required for a shareholder who directly holds ordinary shares to transfer those ordinary 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 ordinary shares may transfer those ordinary shares into his or her own broker account (or vice versa) without giving rise to Irish stamp duty, provided that there is no change in the beneficial ownership of the ordinary shares as a result of the transfer and the transfer is not made in contemplation of a sale of the ordinary shares.

Accordingly, we strongly recommend that shareholders hold their shares through DTC (or through a broker who holds such shares through DTC).

Any transfer of our ordinary shares that is subject to Irish stamp duty will not be registered in the name of the buyer unless such stamp duty is paid and details of the transfer are provided to our transfer agent. Our Articles of Association allow us, in our absolute discretion, to pay (or cause one of our affiliates to pay) any stamp duty. We do not expect to pay any stamp duty on behalf of any acquirer of ordinary shares in our capital. See the section titled “Taxation—Material Irish Tax Considerations.”

Our Articles of Association provide that, in the event of any such payment, we (i) may seek reimbursement from the transferor or transferee (at our discretion), (ii) may set-off the amount of the stamp duty against future dividends payable to the transferor or transferee (at our discretion) and (iii) will have a lien against our shares in respect of which we have paid stamp duty.

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 registration of transfers may be suspended at such times and for such periods, not exceeding 30 days in any year, as our board of directors may from time to time determine (except as may be required by law).

Issuance of Shares

We have the authority, pursuant to our Articles of Association, to increase or reduce our authorized but unissued share capital by ordinary resolution (unless otherwise determined by the Board) by creating additional shares of any class or series. An ordinary resolution of our company requires more than 50% of the votes cast at the shareholder meeting by shareholders entitled to vote at that meeting. 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 will 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 are adopted in substantially the form attached as an exhibit to the registration statement of which this prospectus forms a part. We expect that we will seek to renew such general authority at an annual general meeting before the end of that five-year period.

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.

No Sinking Fund

Our ordinary shares will have no sinking fund provisions.

No Liability for Further Calls or Assessments

The ordinary shares to be sold in this offering will be duly and validly issued, will be credited as fully paid up and will be non-assessable.

Pre-emption Rights, Share Warrants and Share Options

Under Irish law, certain statutory pre-emption rights apply automatically in favor of our ordinary shareholders when our ordinary shares are issued for cash. However, we will opt out of these pre-emption rights in our Articles of Association as permitted under Irish law. This opt-out may be renewed every five years under Irish law by a special resolution of the shareholders. A special resolution requires not less than 75% of the votes cast by our shareholders at a meeting of shareholders. We expect that we will seek renewal of the opt-out at an annual general meeting within five years from the date on which our Articles of Association are adopted in substantially the form attached as an exhibit to the registration statement of which this prospectus forms a part. If the opt-out expires and is not renewed, ordinary shares issued for cash must be offered to our pre-existing ordinary shareholders pro rata based on their existing shareholding before the ordinary shares can be issued to any new shareholders or pre-existing shareholders in an amount greater than their pro rata entitlements. The statutory pre-emption rights:

- generally do not apply where shares are issued for non-cash consideration;
- do not apply to the issuance of non-equity shares (that is, shares that have the right to participate only up to a specified amount in any dividend and capital distribution, which are sometimes referred to as non-participating shares); and
- do not apply to the issuance of shares pursuant to certain employee compensation plans.

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 is authorized, from time to time, in its discretion, to grant such persons, for such periods and upon such terms as the board 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 will be subject to the rules of Nasdaq 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.

Registration Rights

We are party to an investor rights agreement that provides that holders of our preferred shares, including certain officers, holders of 5% of our capital shares and entities affiliated with certain of our directors, have certain registration rights, as set forth below. This investor rights agreement was entered into in November 2015 and has been amended and restated from time to time in connection with our preferred share financings. The registration of our ordinary shares pursuant to the exercise of registration rights described below would enable the holders to sell these shares without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses, other than underwriting discounts and selling commissions, of the shares registered pursuant to the demand, piggyback and Form S-3 registrations described below.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specific conditions, to limit the number of shares such holders may include. The demand, piggyback and Form S-3 registration rights described below will expire after both (i) the effective date of the registration statement, of which this prospectus forms a part, and (ii) all shareholders entitled to registration rights can sell all of their shares under Rule 144 of the Securities Act during any 90-day period.

Demand Registration Rights

The holders of 7,396,313 ordinary shares issuable upon conversion of outstanding preferred shares will be entitled to certain demand registration rights. Beginning after the expiration of the lock-up period on these shares, the holders of a majority of these shares may, on not more than two occasions, request that we file a registration statement having an aggregate offering price to the public of not less than $10,000,000, net of selling expenses, to register the offer and sale of all or a portion of their shares.

Piggyback Registration Rights

In connection with this offering, the holders of 7,809,423 ordinary shares issued or issuable upon the conversion of outstanding preferred shares were entitled to, and the necessary percentage of holders waived, their rights to include their shares of registrable securities in this offering. If we propose to register the offer and sale of any of our securities under the Securities Act either for our own account or for the account of other security holders, the holders of these shares will be entitled to certain “piggyback” registration rights allowing them to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act including a registration statement on Form S-3 as discussed below, other than with respect to a demand registration or a registration statement on Forms S-4 or S-8, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration.

Form S-3 Registration Rights

The holders of 7,396,313 ordinary shares issued or issuable upon the conversion of outstanding preferred shares will be entitled to certain Form S-3 registration rights. The holders of at least 20% of these shares may make a request that we register their shares on Form S-3 if we are qualified to file a registration statement on Form S-3. Such request for registration on Form S-3 must cover securities with an aggregate offering price of at least $1,000,000.

Share Repurchases and Redemptions

Overview

Our Articles of Association provide that any ordinary share we agree to acquire shall be deemed to be a redeemable share. Accordingly, for Irish law purposes, the repurchase of ordinary shares by us may technically be effected as a redemption of those ordinary shares as described below under "Repurchases and Redemptions." If our Articles of Association did not contain such provisions, repurchases by us would be subject to many of the same rules that apply to purchases of our ordinary shares by subsidiaries described below under "Purchases by Subsidiaries," including the shareholder approval requirements described below. Except where otherwise noted, when we refer elsewhere in this prospectus 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 can issue redeemable shares and redeem them out of distributable reserves (which are described below under "Dividends") or the proceeds of a new issue of shares for that purpose. The redemption of redeemable shares may only be made by a public limited company 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. Shareholder approval will not be required to redeem our shares.

The board of directors will also be entitled to issue other classes or series of shares that may be redeemed at the option of either us or the shareholder, depending on the terms of such shares. See the section titled "— 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. While we hold shares as treasury shares, we cannot exercise any voting rights in respect of those shares. Treasury shares may be cancelled by us or re-issued subject to certain conditions.

Purchases by Subsidiaries

Under Irish law, it may be permissible for an Irish or non-Irish subsidiary to purchase our shares. A general authority of our shareholders is required to allow a subsidiary of ours to make on-market purchases of our shares; however, as long as this general authority has been granted, no specific shareholder authority for a particular on-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 our subsidiary, the proposed purchase contract must be authorized by special resolution of our 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 to be proposed, the purchase contract must be on display or must be available for inspection by shareholders at our registered office.

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 our shares, it cannot exercise any voting rights in respect of those shares. The acquisition of our shares by a subsidiary must be funded out of distributable reserves of the subsidiary.

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, less accumulated realized losses of the

company on a standalone basis. In addition, no dividend or distribution may be made unless the net assets of a company are not less than the aggregate of a company's called up share capital plus undistributable reserves and the distribution does not reduce the company's net assets below such aggregate. Undistributable reserves include a company's undenominated capital (effectively its share premium and capital redemption reserve) and the amount by which the company's accumulated unrealized profits, so far as not previously utilized by any capitalization, exceed the company's accumulated unrealized losses, so far as not previously written off in a reduction or reorganization of capital. The determination as to whether or not a company has sufficient distributable reserves to fund a dividend must be made by reference to "relevant accounts" of the company. The "relevant accounts" are either the last set of unconsolidated annual audited financial statements or unaudited financial statements 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. These "relevant accounts" must be filed in the Companies Registration Office (the official public registry for companies in Ireland). Our Articles of Association authorize the board of directors to declare such dividends as appear justified from the profits of the company without the approval of the shareholders. The board of directors may also recommend a dividend to be approved and declared by our shareholders at a general meeting. Our dividends can be declared and paid in the form of cash or non-cash assets, subject to applicable law. We may pay dividends in any currency but, if we elect to pay dividends, we intend to do so in US dollars. Our board of directors may deduct from any dividend or other moneys payable to any shareholder all sums of money, if any, due from the shareholder to the company in respect of ordinary shares of the Company. Our board of directors is also authorized to issue shares in the future with preferred rights to participate in dividends declared by the Company. The holders of such preference shares may, depending on their terms, rank senior to the holders of the ordinary shares of the company with respect to dividends. We do not anticipate paying any cash dividends in the foreseeable future.

For information about the Irish tax considerations relating to dividend payments, see the section titled "Taxation—Irish Tax Considerations."

Bonus Shares

Under our Articles of Association, our board of directors may resolve to capitalize any amount credited to any reserve or fund available for distribution or the share premium account or other of our undistributable reserves for issuance and distribution to shareholders as fully paid up bonus shares on the same basis of entitlement as would apply in respect of a dividend distribution.

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 the allotment, directors may call for any unpaid amounts in respect of any shares to be paid, and if payment is not made, the shares may be forfeited. These provisions are standard inclusions in the articles of association of an Irish company limited by shares such as Iterum and will only be applicable to shares of Iterum that have not been fully paid up.

Consolidation and Division; Subdivision

Under our Articles of Association, we may, by ordinary resolution (unless the board of directors determines otherwise), divide any or all of our share capital into shares of smaller nominal value than its existing shares (often referred to as a share split) or consolidate any or all of our share capital into shares of larger nominal value than its existing shares (often referred to as a reverse share split).

Reduction of Share Capital

We may, by ordinary resolution, reduce our authorized but unissued share capital. We also may, by special resolution and subject to confirmation by the Irish High Court, reduce our issued share capital, and any undenominated share capital.

General Meetings of Shareholders

We are required under Irish law to hold an annual general meeting within 18 months of incorporation and thereafter at intervals of no more than 15 months, provided that an annual general meeting is held in each calendar year 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. Our Articles of Association include a provision requiring annual general meetings to be held within such time periods as required by 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 and 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 to be considered thereat.

Our extraordinary general meetings may be convened (i) by our board of directors, (ii) on requisition of the shareholders holding the number of our shares prescribed by the Irish Companies Act (currently 10% of the paid-up share capital of the Company carrying voting rights), or (iii) in certain circumstances, on requisition of our auditors.

Extraordinary general meetings are generally held for the purposes of approving such of our shareholder resolutions as may be required from time to time. The business to be conducted at any extraordinary general meeting must be set forth in the notice of the meeting.

In the case of an extraordinary general meeting requisitioned by our shareholders, the proposed purpose of the meeting must be set out in the requisition notice of the meeting. The requisition notice can propose any business to be considered at the meeting. Under Irish law, upon receipt of this requisition notice, the board of directors has 21 days to convene the extraordinary general meeting of our shareholders to vote on the matters set out in the requisition notice. This meeting must be held within two months of receipt of the requisition notice. If the board does not proceed to convene the meeting within such 21-day 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 the receipt of the requisition notice by the board.

If our board of directors becomes aware that our net assets are half or less of the amount of our called up share capital, the board must, not later than 28 days from the date that it learns of this fact, convene an extraordinary general meeting of our shareholders 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.

At least 21 days' notice of any annual general meeting or general meeting at which a special resolution is proposed and 14 days in all other circumstances must be given to shareholders, each director and our auditors, under our Articles of Association.

Quorum for Shareholder Meetings

Under our Articles of Association, the presence, in person or by proxy, of one or more shareholders holding not less than a majority of our 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

Generally

Holders of our ordinary shares vote on all matters submitted to a vote of shareholders and are entitled to one vote per share.

All votes at a general meeting will be decided by way of a poll. Voting rights on a poll may be exercised by shareholders registered in our share register as of the record date for the meeting or by a duly appointed proxy of such a registered shareholder, which proxy need not be a shareholder. All proxies must be appointed in accordance with our Articles of Association. Our Articles of Association provide that our board of directors may permit the appointment of proxies by the shareholders to be notified to us electronically.

In accordance with our Articles of Association, our board of directors may, from time to time, cause us to issue preferred or any other class or series of shares. These shares may have such voting rights, if any, as may be specified in the terms of such shares (e.g., they may carry more votes per share or may entitle their holders to a class vote on such matters as may be specified in the terms of the shares).

Treasury shares (i.e., shares held by us) and our shares held by our subsidiaries will not entitle their holders to vote at general meetings of shareholders.

Except where a greater threshold is required by Irish law or our Articles of Association, any question proposed for consideration at any of our general meetings or of any class of shareholders will be decided by an ordinary resolution passed by a simple majority of the votes cast by shareholders entitled to vote at such meeting.

Irish law requires special resolutions of the shareholders at a general meeting to approve certain matters. A special resolution requires not less than 75% of the votes cast by shareholders at a meeting of shareholders.

Examples of matters requiring special resolutions include:

- amending our objects as contained in our Memorandum of Association;
- amending our Articles of Association;
- approving a change of name;
- authorizing the entry into a guarantee or the granting of security in connection with a loan, quasi loan or credit transaction in favor of a director or connected person of a director (which generally includes a family member or business partner of the director and any entity controlled by the director);
- opting out of pre-emption rights on the issuance of new shares;
- re-registering from a public limited company to a private company;

- purchasing of our own shares off-market;
- reducing issued share capital;
- resolving that we be wound up by the Irish courts;
- resolving in favor of a shareholders' voluntary winding-up;
- re-designating shares into different share classes; and
- setting the re-issue price of treasury shares.

Action by Written Consent

Written resolutions by shareholders are not permitted under our Articles of Association.

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 by us 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 in Iterum 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 Dates

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 meeting of the members, which record date shall not be more than sixty (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 sixty (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. 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 10 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 SEC 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 our general meetings and 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) receive copies of financial statements and directors' and auditors' reports which have previously been sent to shareholders prior to an annual general meeting, and (v) 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 audited financial statements 21 days before the 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 company, 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% or more by 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 shareholders 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 offer by a third party pursuant to the Irish Takeover Rules. Where the holders of 80% or more in value of a class of our shares (excluding any shares already beneficially owned by the offeror) have accepted an offer for their shares, the remaining shareholders in that class may be statutorily required to also 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 this "squeeze out" right, the non-accepting shareholders also have a statutory right to require the offeror to acquire their shares on the same terms as the original offer, or such other terms as the offeror and the non-tendering shareholders may agree or on such terms as an Irish court, on application of the offeror or non-tendering shareholder, may order. If our shares were listed on the Irish Stock Exchange or another regulated stock exchange in the European Union, this 80% threshold would be increased to 90%; and
- by way of a merger with a company incorporated in the European Economic Area (EEA) under the European Communities (Cross-Border Mergers) Regulations 2008, which implement the EU Cross Border Merger Directive 2005/56 in Ireland or with another Irish company under the Irish Companies Act. Such a merger must be approved by a special resolution. Shareholders also may be entitled to have their shares acquired for cash. See the section titled "—Appraisal Rights."

The approval of our board of directors, but not shareholder approval, is required for a sale, lease or exchange of all or substantially all of our assets, except that such a transaction between us and one of our directors or a person or entity connected to such a director may require shareholder approval.

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 Mergers) Regulations 2008 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 shareholder, 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 be interested in 3% or more of our shares; or if as a result of a transaction a shareholder who was interested in more than 3% of our shares ceases to be so interested. Where a shareholder is interested in more than 3% of our shares, 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, must be notified to us. The relevant percentage figure is calculated by reference to the aggregate par value of the shares in which the shareholder is interested as a proportion of the entire par value of our share capital. 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 requirement to notify. Where a person fails to comply with the notification requirements described above no right or interest of any kind whatsoever in respect of any of our shares concerned, held by such person, shall be enforceable by such person, whether directly or indirectly, by action or legal proceeding. However, such person may apply to the court to have the rights attaching to the shares concerned reinstated.

In addition to the above disclosure requirement, 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 (a) indicate whether or not it is the case and (b) where such person holds or has during that time held an interest in our shares, to give such further information as may be required by us including particulars of such person's own past or present interests in our shares. Any information given in response to the notice is required to be given in writing within such reasonable time as may be specified in the notice.

Where such a notice is served by us on a person who is or was interested in our shares and that person fails to give us any information required within the reasonable time specified, we may apply to court for an order directing that the affected shares be subject to certain restrictions. Failure to comply with such a court order is a criminal offence.

Under the Irish Companies Act, the restrictions that may be placed on the shares by the court are 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, shall be void;
- no voting rights shall be exercisable in respect of those shares;
- no further shares shall be issued in right of those shares or in pursuance of any offer made to the holder of those shares; and
- no payment shall 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.

Anti-Takeover Provisions

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.

Shareholder Rights Plans and Share Issuances

Irish law does not expressly authorize or prohibit companies from issuing share purchase rights or adopting a shareholder rights plan as an anti-takeover measure; there is no directly relevant case law on this issue. We do not currently have a rights plan in place.

Our Articles of Association expressly authorize our board of directors to adopt a shareholder rights plan, subject to applicable law, including the Irish Takeover Rules and Substantial Acquisition Rules described below and the requirement for shareholder authorization for the issue of shares described above.

Subject to the Irish Takeover Rules described below, our board of directors also has power to issue any of our authorized and unissued shares on such terms and conditions as it may determine and any such action should be taken in the best interests of Iterum. It is possible, however, that the terms and conditions of any issue of preferred shares could discourage a takeover or other transaction that holders of some or a majority of the ordinary shares believe to be in their best interests or in which holders might receive a premium for their shares over the then market price of the shares.

Irish Takeover Rules and Substantial Acquisition Rules

A transaction by virtue of which a third party is seeking 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 classes of shareholders 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 securities in the target company must have sufficient time to allow them to make an informed decision regarding the offer;
- the board of a company must act in the interests of the company as a whole. If the board of the target company advises the holders of securities as regards the offer it must advise on the effects of the implementation of the offer on employment, employment conditions and the locations of the target company's place of business;
- false markets in the securities of the target company or any other company concerned by the offer must not be created;
- a bidder can only announce an offer after ensuring that he or she can fulfill in full the consideration offered;
- a target company may not be hindered longer than is reasonable by an offer for its securities. This is a recognition that an offer will disrupt the day-to-day running of a target company particularly if the offer is hostile and the board of the target company must divert its attention to resist the offer; and
- a "substantial acquisition" of securities (whether such acquisition is to be effected by one transaction or a series of transactions) will only be allowed to take place 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, unless the Irish Takeover Panel otherwise consents, 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 bidder or any of its concert parties acquire our ordinary shares within the period of three months prior to the commencement of the offer period, the offer price must be not less than the highest price paid for our ordinary shares by the bidder or its concert parties during that period. The Irish Takeover Panel has the power to extend the "look back" period to 12 months if the Irish Takeover Panel, having regard to the General Principles, believes it is appropriate to do so.

If the bidder or any of its concert parties 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 shall be in cash (or accompanied by a full cash alternative) and the price per ordinary share shall be not less than the highest price paid by the bidder or its concert parties during, in the case of (i), the period of 12 months 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 its concert parties, 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 Panel, having regard to 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.

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 the board of directors has received an approach which may lead to an offer or has reason to believe an offer is imminent except as noted below. 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 has reason to believe an offer is imminent. Exceptions to this prohibition are available where:

- the action is approved by the offeree at a general meeting; or
- with the consent of the Irish Takeover Panel where:
  - the Irish Takeover Panel is satisfied the action would not constitute a frustrating action;
  - the holders of 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.

For other provisions that could be considered to have an anti-takeover effect, see the sections titled "—Transfer and Registration of Shares," "—Pre-emption Rights, Share Warrants and Share Options," "—Voting—Generally," "—Disclosure of Interests in Shares" and "—Corporate Governance."

Corporate Governance

Generally

Our Articles of Association allocate authority over the management of the Company to our 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. See the section titled "Management—Committees of the Board of Directors."

Directors: Term and Appointment

Directors are elected or appointed at the annual general meeting or at any extraordinary general meeting called for that purpose. Each director is elected by the affirmative vote of a majority of the votes cast with respect to such director. In the event of a "contested election" of directors, directors shall be elected by the vote of a plurality of the votes cast at any meeting for the election of directors at which a quorum is present.

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 holders 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.

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 any such resolution be given to the shareholders 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.

Directors' Duties

Our directors have certain statutory and fiduciary duties. All of the directors have equal and overall responsibility for the management of the Company (although directors who also serve as employees will have additional responsibilities and duties arising under their employment agreements and will be expected to exercise a greater degree of skill and diligence than non-executive directors). The principal fiduciary duties include the statutory and common law fiduciary duties of acting in good faith in the interests of the company and exercising due care and skill. Other statutory duties include ensuring the maintenance of proper books of account, having annual accounts prepared, having an annual audit performed, maintaining certain registers and making certain filings as well as the disclosure of personal interests. Particular duties also apply to directors of insolvent companies (for example, the directors could be liable to sanctions where they are deemed by the court to have carried on our business while insolvent, without due regard to the interests of creditors). For public limited companies, directors are under a specific duty to ensure that the corporate secretary is a person with the requisite knowledge and experience to discharge the role.

Conflicts of Interest

As a matter of Irish law, a director is under a fiduciary duty to avoid conflicts of interest. Irish law and our Articles of Association provide that: (i) a director may be a director of or otherwise interested in a company relating to us and will not be accountable to us for any remuneration or other benefits received as a result, unless we otherwise direct; (ii) a director or a director's firm may act for us in a professional capacity other than as auditor; and (iii) a director may hold an office or place of profit in us and will not be disqualified from contracting with us. If a director has a personal interest in an actual or proposed contract with us, the director must declare the nature of his or her interest and we are required to maintain a register of such declared interests that must be available for inspection by the shareholders. Such a director may vote on any resolution of the board of directors in respect of such a contract, and such a contract will not be voidable solely as a result.

Indemnification of Directors and Officers; Insurance

To the fullest extent permitted by Irish law, our Articles of Association will confer an indemnity on our directors and officers. However, this indemnity is limited by the Irish Companies Act, which prescribes that an advance commitment to indemnify only permits a company to pay the costs or discharge the liability of a director or corporate secretary where judgment is given in favor of the director or corporate secretary in any civil or criminal action in respect of such costs or liability, or where an Irish court grants relief because the director or corporate secretary acted honestly and reasonably and ought fairly to be excused. Any provision whereby an Irish company seeks to commit in advance to indemnify its directors or corporate secretary over and above the limitations imposed by the Irish Companies Act will be void under Irish law, whether contained in its Articles of

Association or any contract between the company and the director or corporate secretary. This restriction does not apply to our executives who are not directors, the corporate secretary or other persons who would be considered "officers" within the meaning of that term under the Irish Companies Act.

Our Articles of Association will also contain indemnification and expense advancement provisions for persons who are not directors or our corporate secretary.

We are permitted under our Articles of Association and the Irish Companies Act to take out directors' and officers' liability insurance, as well as other types of insurance, for our directors, officers, employees and agents.

Additionally, we and certain of our subsidiaries have entered into agreements to indemnify our directors and our executive officers to the maximum extent allowed under applicable law. These agreements, among other things, provide that we will indemnify our directors and executive officers for certain expenses (including attorneys' fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on our behalf or that person's status as our director or executive officer.

Duration; Dissolution; Rights upon Liquidation

Our duration will be unlimited. We may be dissolved at any time by way of either a shareholder's voluntary winding up or a creditors' winding up. In the case of a shareholder's voluntary winding up, the Company must be solvent and a special resolution of the shareholders is required. We may also be dissolved by way of court order on the application of a creditor, or 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 the Company 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, may be prescribed in our Articles of Association or the terms of any shares issued by the board of directors from time to time. 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.

Transfer Agent and Registrar

The transfer agent and registrar for our ordinary shares is Computershare Limited. The transfer agent's address is 1290 Avenue of Americas 9th Floor, New York, New York 10104.

Listing

We have applied to list our ordinary shares on the Nasdaq Global Market under the symbol "ITRM."

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, no public market for our ordinary shares existed, and a liquid trading market for our ordinary shares may not develop or be sustained after this offering. Future sales of our ordinary shares in the public market could adversely affect prevailing market prices of our ordinary shares from time to time and could impair our future ability to raise equity capital in the future. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our ordinary shares in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Based upon the number of shares outstanding as of March 31, 2018, upon the closing of this offering 13,142,756 of our ordinary shares will be outstanding, assuming no exercise of the underwriters' over-allotment option to purchase additional ordinary shares from us and no exercise of outstanding options or warrants. All of the shares sold in this offering will be freely tradable, except that any shares held by our affiliates, as that term is defined in Rule 144 under the Securities Act, may only be sold in compliance with the limitations described below.

The remaining 7,809,423 ordinary shares outstanding after this offering are restricted securities as defined in Rule 144 under the Securities Act or are subject to lock-up agreements with us as described below. Following the expiration of the lock-up period, restricted securities may be sold in the public market only if the offer and sale is registered or if the offer and sale qualifies for an exemption from registration, including under Rule 144 or 701 promulgated under the Securities Act, described in greater detail below. These remaining shares will generally become available for sale in the public market as follows:

- no shares will be eligible for sale in the public market on the date of this prospectus; and
- approximately 7,714,751 shares will be eligible for sale in the public market upon the expiration of lock-up agreements 180 days after the date of this prospectus, subject in certain circumstances to the volume, manner of sale and other limitations of Rule 144 and Rule 701.

Upon the closing of this offering, 19,890 ordinary shares issuable upon exercise of warrants granted by us will be eligible for sale 180 days after the date of this prospectus.

As of March 31, 2018, of the 248,128 ordinary shares issuable upon exercise of options outstanding, approximately 91,251 shares will be vested and eligible for sale 180 days after the date of this prospectus.

We may issue ordinary shares from time to time as consideration for future acquisitions, investments, or other corporate purposes. In the event that any such acquisition, investment, or other transaction is significant, the number of ordinary shares that we may issue may in turn be significant. We may also grant registration rights covering those ordinary shares issued in connection with any such acquisition and investment.

In addition, the ordinary shares reserved for future issuance under our 2018 Plan will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements, a registration statement under the Securities Act or an exemption from registration, including Rule 144 and Rule 701.

Rule 144

In general, persons who have beneficially owned restricted ordinary shares for at least six months, and any affiliate of the company who owns either restricted or unrestricted ordinary shares, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144 under the Securities Act.

Persons who have beneficially owned our restricted ordinary shares for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time

of, or at any time during the 90 days preceding a sale and (ii) we are subject to the periodic reporting requirements of the Exchange Act for at least 90 days before the sale and (iii) we are current in our Exchange Act reporting at the time of sale.

Persons who have beneficially owned our restricted ordinary shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of ordinary shares outstanding after this offering, which will equal approximately 131,427 shares immediately after the closing of this offering, based on the number of ordinary shares outstanding as of March 31, 2018; or
- the average weekly trading volume of our ordinary shares during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale; provided, in each case, that we are subject to the periodic reporting requirements of the Exchange Act for at least 90 days before the sale.

Such sales by affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and in the section of this prospectus titled “Underwriting” and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Regulation S

Regulation S under the Securities Act, as in effect on the date of this prospectus, provides an exemption from registration for certain sales of securities made outside of the United States. Many of our securities sold to non-U.S. shareholders have been issued pursuant to Regulation S. Securities sold pursuant to Regulation S are deemed to be “restricted securities” and any resale of such securities may only be made in accordance with Regulation S, the registration requirements of the Securities Act or an exemption from registration, such as Rule 144 under the Securities Act, which is described above. In general, persons who have beneficially owned our restricted ordinary shares, including shares issued in accordance with Regulation S, and any affiliate of ours who owns either our restricted or unrestricted ordinary shares, including shares issued in accordance with Regulation S, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144 (subject to the volume limitations and other restrictions described above). In addition, our ordinary shares issued in accordance with Regulation S may be resold in accordance with Regulation S or the registration requirements of the Securities Act.

Form S-8 Registration Statements

As soon as practicable after the closing of this offering, we intend to file a Form S-8 registration statement under the Securities Act to register the issuance of our ordinary shares under our equity compensation plans and agreements. This registration statement will become effective immediately upon filing, and shares covered by such registration statement will be eligible for sale in the public markets, subject to vesting restrictions, the lock-up agreements described above and Rule 144 limitations applicable to affiliates. For a more complete discussion of our equity compensation plans, see the section titled “Executive Compensation—Equity Incentive Plans.”

Lock-Up Arrangements

Our officers, directors, and substantially all of our shareholders, option holders and holders of warrants have agreed with the underwriters that for a period of 180 days following the date of this prospectus, subject to certain exceptions, that they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any of our ordinary shares or securities convertible into or exchangeable or exercisable for any of our ordinary shares, enter into a transaction that would have the same effect, or enter into any swap, hedge or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our ordinary shares, whether any of these transactions are to be settled by delivery of our ordinary shares or other securities, in cash or otherwise. Leerink Partners LLC and RBC Capital Markets, LLC may, in their sole discretion, at any time, release all or any portion of the shares from the restrictions in this agreement.

In addition to the restrictions contained in the lock-up agreement described above, we have entered into agreements with certain securityholders, including the investor rights agreement and our standard form option agreement, that contain market stand-off provisions imposing restrictions on the ability of such securityholders to offer, sell, or transfer our equity securities for a period of 180 days following the date of this prospectus.

Registration Rights

Upon the closing of this offering, the holders of 7,809,423 ordinary shares or their transferees, will be entitled to certain rights with respect to the registration of those shares under the Securities Act. If the offer and sale of these shares are registered, they will be freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. For a description of these registration rights, see the section titled “Description of Share Capital—Registration Rights.”

TAXATION

Irish Tax Considerations

Scope of Discussion

The following is a summary of the material Irish tax considerations for certain beneficial owners of our ordinary shares. The summary is based upon Irish tax laws and the practice of the Irish Revenue Commissioners in effect on the date of this prospectus and correspondence with the Irish Revenue Commissioners. Changes in law and/or administrative practice may result in alteration of the tax considerations described below, possibly with retrospective effect.

The summary does not constitute tax advice and is intended only as a general guide. This summary is not exhaustive and shareholders should consult their own tax advisors about the Irish tax consequences (and the tax consequences under the laws of other relevant jurisdictions) which may arise as a result of being a shareholder in our company including the acquisition, ownership and disposition of our ordinary shares. The summary applies only to shareholders who will own our ordinary shares as capital assets and does not apply to other categories of shareholders, such as dealers in securities, trustees, insurance companies, collective investment schemes and shareholders who have, or who are deemed to have, acquired our ordinary shares by virtue of an Irish office or employment (performed or carried on in Ireland).

Tax on Chargeable Gains

The current rate of tax on chargeable gains (where applicable) in Ireland is 33%.

A disposal of our ordinary shares by a shareholder who is not resident or ordinarily resident for tax purposes in Ireland will not give rise to Irish tax on any chargeable gain realized on such disposal unless such shares are used, held or acquired for the purposes of a trade or business carried on by such shareholder through a branch or agency in Ireland.

A holder of our ordinary shares who is an individual and who is temporarily non-resident in Ireland may, under Irish anti-avoidance legislation, be liable to Irish tax on any chargeable gain realized on a disposal of our ordinary shares during the period in which such individual is non-resident.

Stamp Duty

The rate of stamp duty (where applicable) on transfers of shares of Irish incorporated companies is 1% of the price paid or the market value of the shares acquired, whichever is greater. Where Irish stamp duty arises, it is generally a liability of the transferee.

Irish stamp duty may, depending on the manner in which our ordinary shares are held, be payable in respect of transfers of our ordinary shares.

Shares Held through DTC

It is expected that a transfer of our ordinary shares effected by means of the transfer of book entry interests in DTC will not be subject to Irish stamp duty.

Shares Held Outside of DTC or Transferred Into or Out of DTC

A transfer of our ordinary shares where any party to the transfer holds such shares outside of DTC may be subject to Irish stamp duty. Shareholders wishing to transfer their shares into (or out of) DTC may do so without giving rise to Irish stamp duty provided that:

- there is no change in the beneficial ownership of such shares as a result of the transfer; and

- the transfer into (or out of) DTC is not effected in contemplation of a sale of such shares by a beneficial owner to a third party.

Withholding Tax on Dividends Paid on Our Ordinary Shares

As noted elsewhere in this prospectus, we do not expect to pay dividends for the foreseeable future. In addition, our ability to pay dividends is currently restricted by the terms of our secured credit facility with Silicon Valley Bank. To the extent that Iterum does make dividend payments (or other returns to shareholders that are treated as "distributions" for Irish tax purposes), it should be noted that such distributions made by Iterum will, in the absence of one of many exemptions, be subject to Irish dividend withholding tax, which is referred to in this prospectus as "DWT," currently at a rate of 20%.

For DWT purposes, a distribution includes any distribution that may be made by Iterum to its shareholders, including cash dividends, non-cash dividends and additional stock taken in lieu of a cash dividend. Where an exemption does not apply in respect of a distribution made to a particular shareholder, we are responsible for withholding DWT prior to making such distribution.

General Exemptions

The following is a general overview of the scenarios where it will be possible for us to make payments of dividends without deduction of DWT.

Irish domestic law provides that a non-Irish resident shareholder is not subject to DWT on dividends received from Iterum if such shareholder is beneficially entitled to the dividend and is either:

- a person (not being a company) resident for tax purposes in a Relevant Territory (including the United States) and is neither resident nor ordinarily resident in Ireland (for a list of Relevant Territories for DWT purposes as at February 7, 2018, see the section titled "—Relevant Territories for the Purposes of Irish Dividend Withholding Tax");
- a company resident for tax purposes in a Relevant Territory, provided such company is not under the control, whether directly or indirectly, of a person or persons who is or are resident in Ireland;
- a company, wherever resident, that is controlled, directly or indirectly, by persons resident in a Relevant Territory and who is or are (as the case may be) not controlled by, directly or indirectly, persons who are not resident in a Relevant Territory;
- a company, wherever resident, whose principal class of shares (or those of its 75% direct or indirect parent) is substantially and regularly traded on a stock exchange in Ireland, on a recognized stock exchange in a Relevant Territory or on such other stock exchange approved by the Irish Minister for Finance; or
- a company, wherever resident, that is wholly-owned , directly or indirectly, by two or more companies where the principal class of shares of each of such companies is substantially and regularly traded on a stock exchange in Ireland, on a recognized stock exchange in a Relevant Territory or on such other stock exchange approved by the Irish Minister for Finance,

and provided, in all cases noted above, Iterum has received from the shareholder, where required, the relevant Irish Revenue Commissioners DWT form(s) which are referred to in this prospectus as "DWT Forms," prior to the payment of the dividend and such DWT Form(s) remain valid.

For non-Irish resident shareholders that cannot avail themselves of one of Ireland's domestic law exemptions from DWT, it may be possible for such shareholders to rely on the provisions of a double tax treaty to which Ireland is party to reduce the rate of DWT.

Iterum shareholders that do not fall within any of the categories specifically referred to above may nonetheless fall within other exemptions from DWT. If any Iterum shareholders are exempt from DWT, but receive dividends subject to DWT, such shareholders may apply for refunds of such DWT from the Irish Revenue Commissioners.

Income Tax on Dividends Paid on Our Ordinary Shares

Irish income tax may arise for certain persons in respect of dividends received from Irish resident companies. A shareholder that is not resident or ordinarily resident in Ireland and that is entitled to an exemption from DWT generally has no liability to Irish income tax or the universal social charge on a dividend received from us. An exception to this position may apply where such shareholder holds our ordinary shares through a branch or agency in Ireland through which a trade is carried on.

A shareholder that is not resident or ordinarily resident in Ireland and that is not entitled to an exemption from DWT generally has no additional Irish income tax liability or a liability to the universal social charge. The DWT deducted by us discharges the liability to income tax. An exception to this position may apply where the shareholder holds our ordinary shares through a branch or agency in Ireland through which a trade is carried on.

Capital Acquisitions Tax

Irish capital acquisitions tax (CAT) comprises principally gift tax and inheritance 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 are regarded as property situated in Ireland for Irish CAT purposes as our share register must be held in Ireland. The person who receives the gift or inheritance has primary liability for CAT.

CAT is levied at a rate of 33% above certain tax-free thresholds. The appropriate tax free threshold is dependent upon (i) the relationship between the donor and the donee, and (ii) the aggregation of the values of previous gifts and inheritances received by the donee from persons within the same group threshold. Gifts and inheritances passing between spouses of the same marriage or civil partners of the same civil partnership are exempt from CAT. Children have a tax free threshold of €310,000 in respect of taxable gifts or inheritances received from their parents. Our shareholders should consult their own tax advisors as to whether CAT is creditable or deductible in computing any domestic tax liabilities.

There is also a “small gift exemption” from CAT whereby the first €3,000 of the taxable value of all taxable gifts taken by a donee from any one donor, in each calendar year, is exempt from CAT and is also excluded from any future aggregation. This exemption does not apply to an inheritance.

Relevant Territories for the Purposes of Irish Dividend Withholding Tax (as at February 7, 2018)

Albania	Ethiopia	Macedonia	Singapore
Armenia	Finland	Malaysia	Slovak Republic
Australia	France	Malta	Slovenia
Austria	Georgia	Mexico	South Africa
Bahrain	Germany	Moldova	Spain
Belarus	Ghana	Montenegro	Sweden
Belgium	Greece	Morocco	Switzerland
Bosnia & Herzegovina	Hong Kong	Netherlands	Thailand
Botswana	Hungary	New Zealand	The Republic Of Turkey
Bulgaria	Iceland	Norway	Ukraine
Canada	India	Pakistan	United Arab Emirates
Chile	Israel	Panama	United Kingdom
China	Italy	Poland	United States
Croatia	Japan	Portugal	Uzbekistan
Cyprus	Kazakhstan	Qatar	Vietnam
Czech Republic	Korea	Romania	Zambia
Denmark	Kuwait	Russia	
Egypt	Latvia	Saudi Arabia	
Estonia	Lithuania	Serbia	
	Luxembourg		

THE IRISH TAX CONSIDERATIONS SUMMARIZED ABOVE ARE FOR GENERAL INFORMATION ONLY. EACH SHAREHOLDER SHOULD CONSULT HIS OR HER OWN TAX ADVISOR AS TO THE PARTICULAR CONSEQUENCES THAT MAY APPLY TO SUCH SHAREHOLDER.

Material U.S. Federal Income Tax Considerations for U.S. Holders

The following discussion describes the material U.S. federal income tax consequences relating to the ownership and disposition of our ordinary shares by U.S. Holders (as defined below). This discussion applies to U.S. Holders that purchase our ordinary shares pursuant to this offering and hold such ordinary shares as capital assets. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended (the Code), U.S. Treasury regulations promulgated thereunder and administrative and judicial interpretations thereof, all as in effect on the date hereof and all of which are subject to change, possibly with retroactive effect. This discussion does not address all of the U.S. federal income tax consequences that may be relevant to specific U.S. Holders in light of their particular circumstances or to U.S. Holders subject to special treatment under U.S. federal income tax law (such as certain financial institutions; insurance companies; brokers, dealers or traders in securities or other persons that generally mark their securities to market for U.S. federal income tax purposes; tax-exempt entities or governmental organizations; retirement plans; regulated investment companies; real estate investment trusts; grantor trusts; brokers, dealers or traders in commodities, currencies or notional principal contracts; certain former citizens or long-term residents of the United States; persons who hold our ordinary shares as part of a “straddle,” “hedge,” “conversion transaction,” “synthetic security” or integrated investment; persons that have a “functional currency” other than the U.S. dollar; persons that own directly, indirectly or through attribution 10% or more of our ordinary shares; corporations that accumulate earnings to avoid U.S. federal income tax; and partnerships and other pass-through entities and investors in such pass-through entities). This discussion does not address any U.S. state or local or non-U.S. tax consequences or any U.S. federal estate, gift or alternative minimum tax consequences.

- As used in this discussion, 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 an entity treated as a partnership for U.S. federal income tax purposes holds our ordinary shares, the U.S. federal income tax treatment of a partner with respect to an investment in such ordinary shares will depend in part upon the status and activities of such entity and the particular partner. Any such entity, and any partners in such an entity, should consult their own tax advisor regarding the U.S. federal income tax consequences of the purchase, ownership and disposition of our ordinary shares.

Persons considering an investment in our ordinary shares should consult their own tax advisors as to the particular tax consequences applicable to them relating to the purchase, ownership and disposition of our ordinary shares, including the applicability of U.S. federal, state and local tax laws and non-U.S. tax laws.

Passive Foreign Investment Company Consequences

In general, a corporation organized outside the United States will be treated as a passive foreign investment company, or PFIC, for any taxable year in which either (1) at least 75% of its gross income is "passive income" (the PFIC Income Test), or (2) on average at least 50% of its assets, determined on a quarterly basis, are assets that produce passive income or are held for the production of passive income (the PFIC Asset Test). Passive income for this purpose generally includes, among other things, dividends, interest, royalties, rents, and gains from the sale or exchange of property that give rise to passive income. Assets that produce or are held for the production of passive income generally include cash, even if held as working capital or raised in a public offering, marketable securities, and other assets that may produce passive income. Generally, in determining whether a non-U.S. corporation is a PFIC, a proportionate share of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account.

Although PFIC status is determined on an annual basis and generally cannot be determined until the end of the taxable year, based on the nature of our current and expected income and the current and expected value and composition of our assets, we were a PFIC for our 2017 tax year but we do not expect to be a PFIC for our current taxable year. In part, because we may hold a substantial amount of cash and cash equivalents following this offering, and because the calculation of the value of our assets after this offering may be based in part on the value of our ordinary shares, which may fluctuate considerably, there can be no assurance that we will not be a PFIC in future taxable years. Even if we determine that we are not a PFIC for a taxable year, there can be no assurance that the Internal Revenue Service (the IRS) will agree with our conclusion and that the IRS would not successfully challenge our position. Because of the uncertainties involved in establishing our PFIC status, our U.S. counsel expresses no opinion regarding our PFIC status.

If we are a PFIC in any taxable year during which a U.S. Holder owns our ordinary shares, the U.S. Holder could be liable for additional taxes and interest charges under the "PFIC excess distribution regime" upon (1) a distribution paid during a taxable year that is greater than 125% of the average annual distributions paid in the three preceding taxable years, or, if shorter, the U.S. Holder's holding period for our ordinary shares, and (2) any gain recognized on a sale, exchange or other disposition (including, in certain circumstances, a pledge) of our ordinary shares, whether or not we continue to be a PFIC. Under the PFIC excess distribution regime, the tax on such distribution or gain would be determined by allocating the distribution or gain ratably over the U.S. Holder's holding period for our ordinary shares. The amount allocated to the current taxable year (i.e., the year in which the distribution occurs or the gain is recognized) and any year prior to the first taxable year in which we are a PFIC will be taxed as ordinary income earned in the current taxable year. The amount allocated to other taxable years will be taxed at the highest marginal rates in effect for individuals or corporations, as applicable, to ordinary income for each such taxable year, and an interest charge, generally applicable to underpayments of tax, will be added to the tax.

If we are a PFIC for any year during which a U.S. Holder holds our ordinary shares, we must generally continue to be treated as a PFIC by that holder for all succeeding years during which the U.S. Holder holds such ordinary shares, unless we cease to meet the requirements for PFIC status and the U.S. Holder makes a "deemed sale" election with respect to our ordinary shares. If the election is made, the U.S. Holder will be deemed to sell our ordinary shares it holds at their fair market value on the last day of the last taxable year in which we qualified as a PFIC, and any gain recognized from such deemed sale would be taxed under the PFIC excess distribution regime, as described above. After the deemed sale election, the U.S. Holder's ordinary shares will not be treated as shares of a PFIC unless we subsequently become a PFIC.

If we are a PFIC for any taxable year during which a U.S. Holder holds our ordinary shares and one of our non-United States subsidiaries is also 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 PFIC 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 we are a PFIC, a U.S. Holder will not be subject to tax under the PFIC excess distribution regime on distributions or gain recognized on our ordinary shares if a valid "mark-to-market" election is made by the U.S. Holder for our ordinary shares. An electing U.S. Holder generally would take into account as ordinary income each year, the excess of the fair market value of our ordinary shares held at the end of such taxable year over the adjusted tax basis of such ordinary shares. The U.S. Holder would also take into account, as an ordinary loss each year, the excess of the adjusted tax basis of such ordinary shares over those shares' fair market value at the end of the taxable year, but only to the extent of the excess of amounts previously included in income over ordinary losses deducted as a result of the mark-to-market election. The U.S. Holder's tax basis in our ordinary shares would be adjusted to reflect any income or loss recognized as a result of the mark-to-market election. Any gain from a sale, exchange or other disposition of our ordinary shares in any taxable year in which we are a PFIC would be treated as ordinary income and any loss from such sale, exchange or other disposition would be treated first as ordinary loss (to the extent of any net mark-to-market gains previously included in income) and thereafter as capital loss. If, after having been a PFIC for a taxable year, we cease to be classified as a PFIC because we no longer meet the PFIC Income Test or PFIC Asset Test, the U.S. Holder would not be required to take into account any latent gain or loss in the manner described above and any gain or loss recognized on the sale or exchange of the ordinary shares would be classified as a capital gain or loss.

A mark-to-market election is available to a U.S. Holder only for "marketable stock." Generally, stock will be considered marketable stock if it is "regularly traded" on a "qualified exchange" within the meaning of applicable U.S. Treasury regulations. A class of stock is regularly traded during any calendar year during which such class of stock is traded, other than in de minimis quantities, on at least 15 days during each calendar quarter.

Our ordinary shares will be marketable stock as long as they remain listed on Nasdaq and are regularly traded. A mark-to-market election will not apply to the ordinary shares for any taxable year during which we are not a PFIC, but will remain in effect with respect to any subsequent taxable year in which we become a PFIC. Such election will not apply to any of our non-U.S. subsidiaries. Accordingly, a U.S. Holder may continue to be subject to tax under the PFIC excess distribution regime with respect to any lower-tier PFICs notwithstanding the U.S. Holder's mark-to-market election for the ordinary shares.

The tax consequences that would apply if we are a PFIC would also be different from those described above if a U.S. Holder were able to make a valid qualified electing fund (QEF) election. As we do not expect to provide U.S. Holders with the information necessary for a U.S. Holder to make a QEF election, prospective investors should assume that a QEF election will not be available.

The U.S. federal income tax rules relating to PFICs are very complex. Prospective U.S. investors are strongly urged to consult their own tax advisors with respect to the impact of the purchase, ownership and

disposition of our ordinary shares, the consequences to them of an investment in a PFIC, any elections available with respect to the ordinary shares and the IRS information reporting obligations with respect to the purchase, ownership and disposition of ordinary shares of a PFIC.

Distributions

Subject to the discussion above under "—Passive Foreign Investment Company Consequences," a U.S. Holder that receives a distribution with respect to our ordinary shares generally will be required to include the gross amount of such distribution in gross income as a dividend when actually or constructively received by the U.S. Holder to the extent of the U.S. Holder's pro rata share of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). To the extent a distribution received by a U.S. Holder is not a dividend because it exceeds the U.S. Holder's pro rata share of our current and accumulated earnings and profits, it will be treated first as a tax-free return of capital and reduce (but not below zero) the adjusted tax basis of the U.S. Holder's ordinary shares. To the extent the distribution exceeds the adjusted tax basis of the U.S. Holder's ordinary shares, the remainder will be taxed as capital gain. Because we may not account for our earnings and profits in accordance with U.S. federal income tax principles, U.S. Holders should expect all distributions to be reported to them as dividends. The amount of a dividend will include any amounts withheld by the Company in respect of Irish taxes.

Subject to applicable limitations, some of which vary depending upon the U.S. Holder's particular circumstances, Irish income taxes withheld from dividends on the ordinary shares at a rate not exceeding the rate provided by the income tax treaty between Ireland and the United States will be creditable against the U.S. Holder's U.S. federal income tax liability. The rules governing foreign tax credits are complex and U.S. Holders should consult their tax advisors regarding the creditability of foreign taxes in their particular circumstances. In lieu of claiming a foreign tax credit, U.S. Holders may, at their election, deduct foreign taxes, including any Irish income tax withheld from dividends on ordinary shares. An election to deduct foreign taxes instead of claiming foreign tax credits applies to all foreign taxes paid or accrued by a taxpayer in a taxable year.

Distributions on our ordinary shares that are treated as dividends generally will constitute income from sources outside the United States for foreign tax credit purposes and generally will constitute passive category income. Such dividends will not be eligible for the "dividends received" deduction generally allowed to corporate shareholders with respect to dividends received from U.S. corporations. Dividends paid by a "qualified foreign corporation" are eligible for taxation at a reduced capital gains rate rather than the marginal tax rates generally applicable to ordinary income provided that a holding period requirement (more than 60 days of ownership, without protection from the risk of loss, during the 121-day period beginning 60 days before the ex-dividend date) and certain other requirements are met. Each U.S. Holder is advised to consult its tax advisor regarding the availability of the reduced tax rate on dividends. However, if we are a PFIC for the taxable year in which the dividend is paid or the preceding taxable year, we will not be treated as a qualified foreign corporation, and therefore the reduced capital gains tax rate described above will not apply. See the discussion above under "—Passive Foreign Investment Company Consequences.

A non-United States corporation (other than a corporation that is classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation with respect to any dividend it pays on ordinary shares if (i) such foreign corporation is eligible for benefits under a comprehensive income tax treaty that the IRS determines is satisfactory and that includes an exchange of information program and (ii) such ordinary shares are readily tradable on an established securities market in the United States.

Sale, Exchange or Other Disposition of Our Ordinary Shares

Subject to the discussion above under "—Passive Foreign Investment Company Consequences," a U.S. Holder generally will recognize capital gain or loss for U.S. federal income tax purposes upon the sale, exchange

or other disposition of our ordinary shares in an amount equal to the difference, if any, between the amount realized (i.e., the amount of cash plus the fair market value of any property received) on the sale, exchange or other disposition and such U.S. Holder's adjusted tax basis in the ordinary shares. Such capital gain or loss generally will be long-term capital gain taxable at a reduced rate for non-corporate U.S. Holders or long-term capital loss if, on the date of sale, exchange or other disposition, the ordinary shares are held by the U.S. Holder for more than one year. Any capital gain of a non-corporate U.S. Holder that is not long-term capital gain is taxed at ordinary income rates. The deductibility of capital losses is subject to limitations. Any gain or loss recognized from the sale or other disposition of our ordinary shares will generally be gain or loss from sources within the United States for U.S. foreign tax credit purposes.

Medicare Tax

Certain U.S. Holders that are individuals, estates or trusts and whose income exceeds certain thresholds generally are subject to a 3.8% tax on all or a portion of their net investment income, which may include their gross dividend income and net gains from the disposition of our ordinary shares. If you are a United States person that is an individual, estate or trust, you are encouraged to consult your tax advisors regarding the applicability of this Medicare tax to your income and gains in respect of your investment in our ordinary shares.

Information Reporting and Backup Withholding

U.S. Holders may be required to file certain U.S. information reporting returns with the IRS with respect to an investment in our ordinary shares, including, among others, IRS Form 8938 (Statement of Specified Foreign Financial Assets). As described above under "Passive Foreign Investment Company Consequences," each U.S. Holder who is a shareholder of a PFIC must file an annual report containing certain information. U.S. Holders paying more than $100,000 for our ordinary shares may be required to file IRS Form 926 (Return by a U.S. Transferor of Property to a Foreign Corporation) reporting this payment. Substantial penalties may be imposed upon a U.S. Holder that fails to comply with the required information reporting.

Dividends on and proceeds from the sale or other disposition of our ordinary shares may be reported to the IRS unless the U.S. Holder establishes a basis for exemption. Backup withholding may apply to amounts subject to reporting if the holder (1) fails to provide an accurate U.S. taxpayer identification number or otherwise establish a basis for exemption, or (2) is described in certain other categories of persons. However, U.S. Holders that are corporations generally are excluded from these information reporting and backup withholding tax rules.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules generally will be allowed as a refund or a credit against a U.S. Holder's U.S. federal income tax liability if the required information is furnished by the U.S. Holder on a timely basis to the IRS.

U.S. Holders should consult their own tax advisors regarding the backup withholding tax and information reporting rules.

EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT OF AN INVESTMENT IN OUR ORDINARY SHARES IN LIGHT OF THE INVESTOR'S OWN CIRCUMSTANCES. IN ADDITION, SIGNIFICANT CHANGES IN U.S. FEDERAL INCOME TAX LAWS WERE RECENTLY ENACTED. PROSPECTIVE INVESTORS SHOULD ALSO CONSULT WITH THEIR TAX ADVISORS WITH RESPECT TO SUCH CHANGES IN U.S. TAX LAW AS WELL AS POTENTIAL CONFORMING CHANGES IN STATE TAX LAWS.

UNDERWRITING

Leerink Partners LLC and RBC Capital Markets, LLC are acting as representatives of each of the underwriters named below and as joint bookrunning managers for this offering. Subject to the terms and conditions set forth in the underwriting agreement among us and the underwriters, we have agreed to issue to the underwriters, and each of the underwriters has agreed, severally and not jointly, to subscribe for, the number of ordinary shares set forth opposite its name below.

Underwriter	Number of Shares
Leerink Partners LLC	
RBC Capital Markets, LLC	
Guggenheim Securities, LLC	
Needham & Company, LLC	
Total	5,333,333

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to subscribe for all of the shares (other than those covered by the over-allotment option described below) issuable under the underwriting agreement if they subscribe for any of the shares. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of $ per share. After the initial offering of the shares, the public offering price, concession or any other term of the offering may be changed by the representatives.

The following table shows the public offering price, underwriting discounts and commissions and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their over-allotment option.

	Per Share		Total	
	Without Option	With Option	Without Option	With Option
Public offering price	$	$	$	$
Underwriting discounts and commissions				
Proceeds, before expenses, to us				

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $3.0 million. We also have agreed to reimburse the underwriters for up to $35,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Over-Allotment Option

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to subscribe for up to 799,999 additional shares at the public offering price, less the underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to conditions contained in the underwriting agreement, to subscribe for a number of additional shares proportionate to that underwriter's initial amount reflected in the above table. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the ordinary shares offered by this prospectus.

No Sales of Similar Securities

We, our executive officers and directors and all of our other existing shareholders have agreed not to sell or transfer any ordinary shares or securities convertible into or exchangeable or exercisable for ordinary shares, for 180 days after the date of this prospectus without first obtaining the written consent of Leerink Partners LLC and RBC Capital Markets, LLC on behalf of the underwriters. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any ordinary shares;
- sell any option or contract to purchase any ordinary shares;
- purchase any option or contract to sell any ordinary shares;
- grant any option, right or warrant for the sale of any ordinary shares;
- otherwise dispose of or transfer any ordinary shares;
- request or demand that we file a registration statement related to the ordinary shares; or
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of any ordinary shares, whether any such swap, agreement or transaction is to be settled by delivery of ordinary shares or other securities, in cash or otherwise.

This lock-up provision applies to ordinary shares and to securities convertible into or exchangeable or exercisable for ordinary shares. It also applies to ordinary shares owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

Nasdaq Global Market Listing

We have applied to list our ordinary shares on the Nasdaq Global Market, subject to notice of issuance, under the symbol "ITRM."

Determination of Offering Price

Before this offering, there has been no public market for our ordinary shares. The initial public offering price will be determined through negotiations between us and the representatives. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are:

- the valuation multiples of publicly traded companies that the representatives believe to be comparable to us;
- our financial information;
- the history of, and the prospects for, our company and the industry in which we compete;
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues;

- the present state of our development; and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our ordinary shares. However, the representatives may engage in transactions that stabilize the price of the ordinary shares, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our ordinary shares in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales, which may include purchases pursuant to the over-allotment option, and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ over-allotment option described above. The underwriters may close out any covered short position by either exercising their over-allotment option or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option granted to them. “Naked” short sales are sales in excess of such over-allotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our ordinary shares in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of ordinary shares made by the underwriters in the open market prior to the closing of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our ordinary shares or preventing or retarding a decline in the market price of our ordinary shares. As a result, the price of our ordinary shares may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our ordinary shares. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and certain of their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, no offer of shares may be made to the public in that Relevant Member State other than:

A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;

B. to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

We, the representatives and each of our and the representatives' and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus

for offers of shares. Accordingly, any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression "an offer to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

MiFID II Product Governance

Any person offering, selling or recommending the shares (a "distributor") should take into consideration the manufacturers' target market assessment; however, a distributor subject to MiFID II is responsible for undertaking its own target market assessment in respect of the shares (by either adopting or refining the manufacturers' target market assessment) and determining appropriate distribution channels.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons") or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority ("FINMA"), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre ("DIFC")

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority ("DFSA"). This document is intended for distribution only to persons of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for this document. The securities to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this document you should consult an authorized financial advisor.

In relation to its use in the DIFC, this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the securities may not be offered or sold directly or indirectly to the public in the DIFC.

Notice to Prospective Investors in the United Arab Emirates

The shares have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Center) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Center) governing the issue, offering and sale of securities. Further, this prospectus does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Center) and is not intended to be a public offer. This prospectus has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Notice to Prospective Investors in Australia

This prospectus:

- does not constitute a product disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth) (the "Corporations Act");

- has not been, and will not be, lodged with the Australian Securities and Investments Commission ("ASIC"), as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document under Chapter 6D.2 of the Corporations Act;
- does not constitute or involve a recommendation to acquire, an offer or invitation for issue or sale, an offer or invitation to arrange the issue or sale, or an issue or sale, of interests to a "retail client" (as defined in section 761G of the Corporations Act and applicable regulations) in Australia; and
- may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, or Exempt Investors, available under section 708 of the Corporations Act.

The shares may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the shares may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any shares may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the shares, you represent and warrant to us that you are an Exempt Investor.

As any offer of shares under this document will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the shares you undertake to us that you will not, for a period of 12 months from the date of issue of the shares, offer, transfer, assign or otherwise alienate those securities to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Notice to Prospective Investors in Japan

The shares have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Act. Accordingly, none of the shares nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any "resident" of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

Notice to Prospective Investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is or will be given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to Prospective Investors in China

This prospectus does not constitute a public offer of shares, whether by sale or subscription, in the People's Republic of China (the "PRC"). The shares are not being offered or sold directly or indirectly in the PRC to or for the benefit of, legal or natural persons of the PRC.

Further, no legal or natural persons of the PRC may directly or indirectly purchase any of the shares or any beneficial interest therein without obtaining all prior PRC's governmental approvals that are required, whether statutorily or otherwise. Persons who come into possession of this document are required by the issuer and its representatives to observe these restrictions.

LEGAL MATTERS

The validity of the ordinary shares being offered by this prospectus will be passed upon for us by A&L Goodbody, Dublin, Ireland. Certain other legal matters relating to this offering will be passed upon for us by Cooley LLP. Certain legal matters in connection with this offering will be passed upon for the underwriters by Davis Polk & Wardwell LLP.

EXPERTS

The consolidated financial statements of Iterum Therapeutics plc (formerly known as Iterum Therapeutics Limited) as of December 31, 2016 and December 31, 2017 and for each of the years in the two-year period ended December 31, 2017, have been included herein in reliance upon the report of KPMG, independent registered public accounting firm, appearing elsewhere herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have submitted with the SEC a registration statement on Form S-1, including exhibits and schedules, under the Securities Act, with respect to the ordinary shares being offered by this prospectus. This prospectus, which constitutes part of the registration statement, does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the ordinary shares offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the internet at the SEC's website at www.sec.gov. You may also read and copy any document we file with the SEC at its public reference facilities at 100 F Street, NE, Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities. You may also request a copy of these filings, at no cost, by writing us at 200 South Wacker Dr., Suite 650, Chicago, IL 60606.

Upon the closing of this offering, we will be subject to the information reporting requirements of the Securities Exchange Act of 1934 and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available for inspection and copying at the public reference room and web site of the SEC referred to above. We also maintain a website at www.iterumtx.com, at which, following the closing of this offering, you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

ITERUM THERAPEUTICS PLC (FORMERLY ITERUM THERAPEUTICS LIMITED)

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

	Page
Report of Independent Registered Public Accounting Firm	F-2
Consolidated Balance Sheets	F-3
Consolidated Statements of Operations and Comprehensive Loss	F-4
Consolidated Statements of Changes in Convertible Preferred Shares and Shareholders' Equity	F-5
Consolidated Statements of Cash Flows	F-6
Notes to Consolidated Financial Statements	F-7

Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors
Iterum Therapeutics plc (formerly Iterum Therapeutics Limited):

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Iterum Therapeutics plc (formerly Iterum Therapeutics Limited) and subsidiaries (the Company) as of December 31, 2016 and 2017, the related consolidated statements of operations and comprehensive loss, changes in convertible preferred shares and shareholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2017, 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, 2016 and 2017, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

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. 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 December 31, 2015.

Dublin, Ireland
March 9, 2018, except for the effects of the Reverse Share Split discussed in Note 12 to the consolidated financial statements, as to which the date is May 16, 2018

ITERUM THERAPEUTICS PLC

Consolidated Balance Sheets

(In thousands, except share and per share data)

	December 31, 2016	December 31, 2017	March 31, 2018	Pro Forma March 31, 2018
			(unaudited)	
Assets				
Current assets:				
Cash and cash equivalents	$ 24,809	$ 8,485	$ 38,258	38,258
Short-term investments	—	30,731	21,376	21,376
Prepaid expenses and other current assets	1,053	4,957	5,751	5,751
Total current assets	25,862	44,173	65,385	65,385
Property and equipment, net	—	747	737	737
Restricted cash	—	—	120	120
Other assets	1,055	1,837	1,889	1,889
Total assets	$ 26,917	$ 46,757	$ 68,131	$ 68,131
Liabilities, Convertible Preferred Shares and Shareholders' Equity				
Current liabilities:				
Accounts payable	$ 1,481	$ 3,152	$ 3,575	$ 3,575
Accrued expenses	2,738	3,974	4,748	4,748
Total current liabilities	4,219	7,126	8,323	8,323
Other liabilities	—	80	78	78
Total liabilities	$ 4,219	$ 7,206	$ 8,401	$ 8,401
Commitments and contingencies (*Note 11*)				
Series A convertible preferred shares, $0.01 par value per share; 3,032,463 shares authorized, 3,032,457 shares issued at December 31, 2016 and 2017 and March 31, 2018 (unaudited); no shares issued at March 31, 2018 pro forma (unaudited)	30	30	30	—
Series B convertible preferred shares, $0.01 par value per share; 3,696,943 shares authorized, 2,654,206 shares issued at December 31, 2017; 4,801,493 shares authorized, 4,363,856 shares issued at March 31, 2018 (unaudited); no shares issued at March 31, 2018 pro forma (unaudited)	—	27	44	—
Shareholders' equity:				
Ordinary shares, $0.01 par value per share; 3,659,453 and 7,956,715 shares authorized at December 31, 2016 and 2017, 413,110 shares issued at December 31, 2016 and 2017; 44,557,606 shares authorized, 413,110 shares issued at March 31, 2018 (unaudited); 7,809,423 shares issued at March 31, 2018 pro forma (unaudited)	4	4	4	78
Additional paid-in capital	47,995	94,227	126,535	126,535
Accumulated deficit	(25,331)	(54,737)	(66,883)	(66,883)
Total shareholders' equity	22,668	39,494	59,656	59,730
Total liabilities, convertible preferred shares and shareholders' equity	$ 26,917	$ 46,757	$ 68,131	$ 68,131

See Accompanying Notes to the 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,		Three Months Ended March 31,	
	2016	2017	2017	2018
			(unaudited)	
Revenue	$ —	$ 508	$ —	$ 191
Operating expenses:				
Research and development	$ (10,101)	$ (25,499)	$ (4,534)	$ (10,879)
General and administrative	(3,258)	(4,464)	(1,008)	(1,515)
Total operating expenses	(13,359)	(29,963)	(5,542)	(12,394)
Operating loss	(13,359)	(29,455)	(5,542)	(12,203)
Interest income, net	—	277	—	85
Other income/(expense), net	8	216	(68)	61
Total other income	8	493	(68)	146
Loss before income taxes	(13,351)	(28,962)	(5,610)	(12,057)
Income tax expense	(113)	(444)	(227)	(89)
Net loss and comprehensive loss	(13,464)	(29,406)	(5,837)	(12,146)
Net loss attributable to ordinary shareholders	$ (13,464)	$ (29,406)	$ (5,837)	$ (12,146)
Net loss per share attributable to ordinary shareholders—basic and diluted	$ (568.87)	$ (170.84)	$ (103.68)	$ (61.36)
Weighted average ordinary shares outstanding—basic and diluted	23,668	172,130	56,301	197,949
Pro forma net loss per share attributable to ordinary shareholders—basic and diluted (unaudited)		$ (5.02)		$ (1.60)
Pro forma weighted average ordinary shares outstanding—basic and diluted (unaudited)		5,858,793		7,594,262

See Accompanying Notes to the Consolidated Financial Statements

ITERUM THERAPEUTICS PLC

Consolidated Statements of Changes in Convertible Preferred Shares and Shareholders' Equity

(In thousands, except share and per share data)

	Convertible Preferred Shares		Ordinary Shares		Preferred Shares to be Issued	Additional Paid in Capital	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount				
Balance, December 31, 2015	1,514,320	$ 15	413,110	$ 4	$ 3,000	$ 23,813	$ (11,867)	$ 14,950
Issuance of Series A convertible preferred shares	1,518,137	15	—	—	(3,000)	23,834	—	20,834
Share-based compensation expense	—	—	—	—	—	348	—	348
Net loss	—	—	—	—	—	—	(13,464)	(13,464)
Balance, 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, December 31, 2017	5,686,663	$ 57	413,110	$ 4	$ —	$ 94,227	$ (54,737)	$ 39,494
Issuance of Series B convertible preferred shares, net	1,709,650	17	—	—	—	32,159	—	32,159
Share-based compensation expense	—	—	—	—	—	149	—	149
Net loss	—	—	—	—	—	—	(12,146)	(12,146)
Balance, March 31, 2018 (unaudited)	7,396,313	$ 74	413,110	$ 4	$ —	$ 126,535	$ (66,883)	$ 59,656

See Accompanying Notes to the Consolidated Financial Statements

ITERUM THERAPEUTICS PLC

Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31, 2016	Year Ended December 31, 2017	Three Months Ended March 31, 2017	Three Months Ended March 31, 2018
			(unaudited)	
Cash flows from operating activities:				
Net loss	$ (13,464)	$ (29,406)	$ (5,837)	$(12,146)
Adjustments to reconcile net loss to cash used in operating activities:				
Depreciation	—	65	—	31
Share-based compensation expense	348	392	89	149
Non-cash loss on short-term investments	—	44	—	(23)
Interest on short-term investments	—	(95)	—	—
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(966)	(3,815)	(246)	(793)
Other assets	(1,052)	(782)	(464)	(52)
Accounts payable	1,188	1,671	(361)	422
Accrued expenses	2,665	1,236	1,099	692
Income taxes	(17)	6	198	82
Other liabilities	—	80	87	(2)
Net cash used in operating activities	(11,298)	(30,604)	(5,435)	(11,640)
Cash flows from investing activities:				
Purchases of property and equipment	—	(812)	(518)	(21)
Purchases of short-term investments	—	(53,275)	—	(6,372)
Proceeds from sale of short-term investments	—	22,500	—	15,750
Net cash (used in) / provided by investing activities	—	(31,587)	(518)	9,357
Cash flows from financing activities:				
Proceeds from issuance of Series A convertible preferred shares	20,851	—	—	—
Proceeds from issuance of Series B convertible preferred shares	—	45,867	—	32,176
Net cash provided by financing activities	20,851	45,867	—	32,176
Net increase / (decrease) in cash, cash equivalents and restricted cash	9,553	(16,324)	(5,953)	29,893
Cash, cash equivalents and restricted cash, at beginning of period	15,256	24,809	24,809	8,485
Cash, cash equivalents and restricted cash, at end of period	$ 24,809	$ 8,485	$18,856	$ 38,378
Supplemental Disclosure of Cash Flow Information:				
Income tax paid—U.S.	$ 130	$ 439	$ —	$ —

See Accompanying Notes to the Consolidated Financial Statements

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

(1) Nature of Operations and Basis of Presentation

Iterum Therapeutics plc (the "Company") was incorporated under the laws of the state of Ireland in June 2015 as a limited company and re-registered as a plc 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 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 convertible preferred shares. 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, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. 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.

Going Concern

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 incurred operating losses since inception, including a net loss of $5,837 and $12,146 for the periods ended March 31, 2017 and March 31, 2018, respectively and a net loss of $13,464 and $29,406 for the years end December 31, 2016 and December 31, 2017 respectively. The Company had an accumulated deficit of $66,883 as of March 31, 2018. The Company expects to continue to incur net losses for the next several years and is highly dependent on its ability to find additional sources of funding in the form of debt or equity financing to fund its operations. Management believe that its cash and cash equivalents balance of $38,258 and short-term investments balance of $21,376 at March 31, 2018, together with the $15,000 loan drawn down from a secured credit facility with Silicon Valley Bank in April 2018, are sufficient to fund operations for at least one year from the date the consolidated financial statements are issued. In making this assessment management have considered the future financing options available to the Company, the planned operations of the Company and the ability to adjust its plans if required.

The Company will be required to obtain additional funding in order to continue to fund its operations after at least one year from the date the consolidated financial statements are issued and intends to pursue a public offering of its ordinary shares to fund future operations. However, if the Company is unable to complete a sufficient public offering in a timely manner it would need to pursue other financing alternatives including

private financing of debt or equity or collaboration agreements. There can be no assurances, however, that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all.

(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, revenue from grant awards, 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.

Unaudited Interim Financial Information

The accompanying consolidated balance sheet as of March 31, 2018, the consolidated statements of operations and comprehensive loss and the consolidated statements of cash flows for the three months ended March 31, 2017 and 2018, and the consolidated statement of changes in convertible preferred shares and shareholders' equity for the three months ended March 31, 2018 are unaudited. The unaudited interim consolidated financial statements have been prepared on the same basis as the audited annual consolidated financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for the fair statement of the Company's financial position as of March 31, 2018 and the results of its operations and its cash flows for the three months ended March 31, 2017 and 2018. The financial data and other information disclosed in these notes related to the three months ended March 31, 2017 and 2018 are also unaudited. The results for the three months ended March 31, 2018 are not necessarily indicative of results to be expected for the year ending December 31, 2018, any other interim periods, or any future year or period.

Unaudited Pro Forma Information

The accompanying unaudited pro forma consolidated balance sheet as of March 31, 2018 has been prepared to give effect, upon the closing of a qualified Initial Public Offering (IPO) (see *Note 8*), to the automatic conversion of all shares of convertible preferred shares outstanding as of March 31, 2018 into 7,396,313 ordinary shares as if the proposed IPO had occurred on March 31, 2018. In the accompanying consolidated statements of operations and comprehensive loss, the unaudited pro forma basic and diluted net loss per share attributable to ordinary shareholders for the year ended December 31, 2017 and the three months ended March 31, 2018 have been prepared to give effect, upon the closing of a qualified IPO, to the automatic conversion of all shares of convertible preferred shares into ordinary shares as if the proposed IPO had occurred on the later of January 1, 2017 or the issuance date of the convertible preferred shares.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in shareholders' 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 (collectively, the "Company"). 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 FASB 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 €100 ($123).

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 $120 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 11, 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.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

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:

Asset class	Years
Leasehold improvements	Shorter of lease term or 10 years
Furniture and fixtures	5
Laboratory equipment	5
Computer equipment	3

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.

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 both inside and outside of Ireland. 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 and clinical studies; and
- Contract Manufacturing Organizations, or CMOs, in connection with drug substance and drug product formulation of preclinical and clinical trial materials.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

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 all share-based awards granted to employees and directors 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. The Company issues awards with only service based vesting conditions and records the expense for these awards 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.

The Company classifies share-based compensation expense in its 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. 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. There have been no forfeitures through March 31, 2018.

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 a sub-award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator ("CARB-X") program (the "CARB-X award") in the amount of $1,497. The CARB-X award is structured as a cost reimbursement arrangement and is being recognized over a period of 20 months from August 2017.

The Company recognizes the CARB-X award as revenue, rather than as a reduction of research and development expenses, because the Company is the principal in conducting the research and development activities and this contract is central to its ongoing operations. Revenue is recognized as the qualifying expenses related to the contract are incurred. Revenue recognition commences only once persuasive evidence of a contract exists, services have been rendered, the reimbursement amounts under the contract are fixed or determinable, and collectability is reasonably assured. 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 are included in research and development expenses in the Company's consolidated statements of operations and comprehensive loss. There was no revenue recognized for the year ended December 31, 2016. $508 and $191 was recognized as revenue for the year ended December 31, 2017 and for the period ended March 31, 2018, respectively.

Research and Development Credits

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

Deferred Transaction Costs

Deferred transaction costs primarily consist of direct incremental legal, accounting, and other fees relating to the Company's contemplated IPO and are capitalized as incurred. The deferred transaction costs will be offset against IPO proceeds upon the consummation of the offering. In the event the IPO is terminated, which would include a postponement of 90 days or greater, any deferred transaction costs will be expensed. There were no transaction costs deferred as of December 31, 2016. Transaction costs of $180 and $1,615 were deferred as of December 31, 2017 and March 31, 2018, respectively, and are included within prepaid expenses and other current assets in the accompanying consolidated balance sheets.

Fair Value of Financial Instruments

Financial Accounting Standards Board ("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.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

- 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.

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 and short-term investments at two accredited financial institutions in the United States, in amounts that exceed federally insured limits. 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 is greater than 50% likely 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.

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 and options, and unvested restricted ordinary shares have been excluded from the calculation because they would be anti-dilutive.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

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,		Three Months Ended March 31,	
	2016	2017	2017	2018
			(unaudited)	
Options to purchase ordinary shares	49,330	248,128	63,650	248,128
Preferred shares convertible into ordinary shares	3,032,457	5,686,663	3,032,457	7,396,313
Unvested restricted ordinary shares	292,620	189,342	266,800	163,523
Total	3,374,407	6,124,133	3,362,907	7,807,964

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

Segment Information

The Company determines and presents operating segments based on the information that is internally provided to the Chief Executive Officer, Chief Scientific Officer, Chief Financial Officer and Chief Commercial 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:

Operating expenses	Year Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
			(unaudited)	
Ireland	$ 9,864	$24,619	4,469	9,964
U.S.	3,495	5,344	1,073	2,430
Total	$13,359	$29,963	5,542	12,394

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

Long-lived assets	December 31, 2016	December 31, 2017	March 31, 2018
			(unaudited)
Ireland	$ 1,044	$ 2,341	2,378
U.S.	11	243	368
Total	$ 1,055	$ 2,584	2,746

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. The Company is required to contribute a deferral rate of up to 3% to the 401(k) Plan on behalf of certain employees.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

Inventory

Inventories are valued at the lower of cost or market. 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 purchases of the API and the manufacturing of the product candidate 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, 2016, December 31, 2017 or March 31, 2018.

Contingent Consideration

Certain licence agreements contain milestone payments that could result in the requirement to make contingent consideration payments, see *Note 11* 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.

Recent Accounting Pronouncements

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 is not expected to have a significant impact on the consolidated financial statements.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842*). ASU 2016-02 was issued to increase transparency and comparability among entities by recognizing lease assets and lease liabilities on the consolidated balance sheet and disclosing key information about lease arrangements. ASU 2016-02 is effective for public companies for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2018. The Company is currently evaluating the impact of adopting ASU 2016-02 on the consolidated financial statements.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

In March 2017, the FASB issued ASU 2017-07, Compensation—Retirement Benefits (Topic 715): Improving the Presentation of Net Periodic Pension Cost and Net Periodic Postretirement Benefit Cost, which requires companies to present the service cost component of net benefit cost in the same line items in which they report compensation cost. Companies will present all other components of net benefit cost outside operating income, if this subtotal is presented. This ASU is effective for public business entities for annual and interim periods in fiscal years beginning after December 15, 2017. The adoption of ASU 2017-07 did not have an impact on the Company's consolidated financial statements.

In August 2016, the FASB issued ASU No. 2016-15, Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments ("ASU 2016-15"), to address diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. The adoption of ASU 2016-15 did not have an impact on the Company's consolidated financial statements.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606)* ("ASU 2014-09"), which supersedes existing revenue recognition guidance under GAAP. The standard's core principle is that a company will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those goods or services. The standard defines a five-step process to achieve this principle, and will require companies to use more judgment and make more estimates than under the current guidance. The Company expects that these judgments and estimates will include identifying performance obligations in the customer contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each separate performance obligation. ASU 2014-09 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts. In August 2015, the FASB issued ASU 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, which delays the effective date of ASU 2014-09 such that the standard is effective for public entities for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. In March 2016, the FASB issued ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations* ("ASU 2016-08"), which further clarifies the implementation guidance on principal versus agent considerations in ASU 2014-09. In April 2016, the FASB issued ASU No. 2016-10, *Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing*, clarifying the implementation guidance on identifying performance obligations and licensing. Specifically, the amendments in this update reduce the cost and complexity of identifying promised goods or services and improve the guidance for determining whether promises are separately identifiable. The amendments in this update also provide implementation guidance on determining whether an entity's promise to grant a license provides a customer with either a right to use the entity's intellectual property (which is satisfied at a point in time) or a right to access the entity's intellectual property (which is satisfied over time). In May 2016, the FASB issued ASU No. 2016-12, *Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients* ("ASU 2016-12"), which clarifies the objective of the collectability criterion, presentation of taxes collected from customers, non-cash consideration, contract modifications at transition, completed contracts at transition and how guidance in ASU 2014-09 is retrospectively applied. ASU 2016-08, ASU 2016-10 and ASU 2016-12 have the same effective dates and transition requirements as ASU 2014-09. The Company determined that the CARB-X award is outside the scope of ASC 606. Therefore, the adoption of ASC 606 did not impact the Company's consolidated financial statements as the only revenue currently being recorded by the Company as of March 31, 2018 is the sub-award granted by CARB-X.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

(3) Fair Value of Financial Assets

The following table presents information about the Company's financial assets that have been measured at fair value at December 31, 2016, December 31, 2017 and March 31, 2018 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value.

December 31, 2016

Assets	Total	Level 1	Level 2	Level 3
Other asset—advance payment to supplier	$740	—	—	740
Total	$740	—	—	740

December 31, 2017

Assets	Total	Level 1	Level 2	Level 3
Short-term investments	$30,731	30,731	—	—
Other asset—advance payments to supplier	1,472	—	—	1,472
Total	$32,203	30,731	—	1,472

March 31, 2018 (unaudited)

Assets	Total	Level 1	Level 2	Level 3
Short-term investments	21,376	21,376	—	—
Other asset—advance payments to supplier	1,515	—	—	1,515
Total	22,891	21,376	—	1,515

See *Note 4* for further details on the short-term investments held. 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, 2016, December 31, 2017 and March 31, 2018. Key assumptions used in the DCF include a discount rate of 15% and the expected time to recovery of the payment. See *Note 11—Payment to Supplier,* for further details on these advance payments.

(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 and as at period-end consist of U.S. Treasury and agency bonds and corporate entity commercial paper with maturities of more than three months but less than one year at the date of purchase. Short-term investments as of March 31, 2018 have an average maturity of 0.17 years. The 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 value 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 available for sale securities as of December 31, 2016.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

The following table represents the Company's available for sale short-term investments by major security type as of December 31, 2017 and March 31, 2018:

December 31, 2017					Maturity by period	
Available for sale	Cost Total	Unrealized gains	Unrealized (losses)	Fair Value Total	Less than 1 year	1 to 5 years
Commercial paper	$22,538	8	(27)	22,519	22,519	—
U.S. Treasury and Agency Bonds	8,205	18	(11)	8,212	8,212	—
Total	$30,743	26	(38)	30,731	30,731	—

March 31, 2018 (unaudited)					Maturity by period	
Available for sale	Cost Total	Unrealized gains	Unrealized (losses)	Fair Value Total	Less than 1 year	1 to 5 years
Commercial paper	$14,755	28	(15)	14,768	14,768	—
U.S. Treasury and Agency Bonds	6,617	18	(27)	6,608	6,608	—
Total	$21,372	46	(42)	21,376	21,376	—

(5) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following:

	December 31, 2016	December 31, 2017	March 31, 2018 (unaudited)
Prepaid research and development expenses	$ 264	$ 2,289	$ 1,716
Short-term deposits	404	1,346	1,006
Other prepaid assets	63	516	827
Value added tax receivable	245	281	297
Deferred IPO expenses	—	180	1,615
Research and development tax credit receivable	—	133	137
Prepaid insurance	77	117	85
Interest receivable	—	95	68
Total	$ 1,053	$ 4,957	$ 5,751

(6) Property and Equipment, net

Property and equipment and related accumulated depreciation are as follows:

	December 31, 2016	December 31, 2017	March 31, 2018 (unaudited)
Leasehold improvements	$ —	$ 579	$ 579
Furniture and fixtures	—	108	112
Laboratory equipment	—	81	81
Computer equipment	—	44	61
	—	812	833
Less: accumulated depreciation	—	(65)	(96)
	$ —	$ 747	$ 737

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

Depreciation expense was $65 for the year ended December 31, 2017 and $31 for the three month period ended March 31, 2018. There was no depreciation expense for the year ended December 31, 2016.

(7) Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2016	December 31, 2017	March 31, 2018 (unaudited)
Accrued manufacturing expenses	$ 1,373	$ 2,031	$ 2,355
Accrued payroll and bonus expenses	789	1,059	482
Accrued clinical trial costs	426	594	978
Accrued other expenses	150	290	933
Total	$ 2,738	$ 3,974	4,748

(8) Shareholders' Equity

The Company's capital structure consists of ordinary shares and 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.

Ordinary Shares

The Company was initially incorporated without a cap on its authorized share capital as permitted by the Companies Act 2014 of Ireland. On October 14, 2015, the Company authorized and issued 413,110 ordinary shares of $0.01 each (after taking account of the reverse share split and redenomination of the ordinary shares from $0.0157 (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 Companies Act 2014 in Ireland.

On November 18, 2015, the Company increased the authorized ordinary share capital to 3,659,453 shares of $0.01 each.

On May 18, 2017, the Company increased the authorized ordinary share capital to 7,956,715 shares of $0.01 each.

On February 16, 2018, the Company increased its authorized ordinary shares by 36,600,891 to 44,557,606 ordinary shares of $0.01 each.

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. The ordinary shares are subordinate to the convertible preferred shares with respect to dividend rights and rights upon liquidation, winding up and dissolution of the Company. The holders of ordinary shares are entitled to liquidation proceeds after all liquidation preferences for the convertible preferred shares are satisfied.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

Convertible Preferred Shares

On November 18, 2015, the Company authorized 3,022,915 Series A convertible preferred shares of $0.01 each. On the same day, the Company issued 1,514,320 Series A convertible preferred shares for $15.71 each for: (1) gross cash proceeds of $20,701; (2) the issue of 190,961 convertible preferred shares to Pfizer as part consideration for the licence agreement; and (3) the conversion of $90 debt owed by the Company to the founders for a total of 5,728 preferred shares (after taking account of the reverse share split and redenomination of the convertible preferred shares from $0.0157 (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 per share in accordance with section 83(1)(c) of the Companies Act 2014 in Ireland.

On December 9, 2016, the Company authorized 9,548 Series A convertible preferred shares of $0.01 each.

On December 16, 2016, the Company issued 1,518,137 Series A convertible preferred shares for $15.71 each 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 of $0.01 each and 1,042,728 Series B-2 convertible preferred shares of $0.01 each (the “Series B convertible preferred shares”). On the same day, the Company issued 2,654,206 Series B-1 convertible preferred shares for $17.28 each, for gross cash proceeds of $45,867 (after taking account of the reverse share split and redenomination of the convertible preferred shares from $0.0157 (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 per share in accordance with section 83(1)(c) of the Companies Act 2014 in Ireland.

On February 16, 2018, the Company increased its authorized Series B-2 convertible preferred shares to 2,147,278 shares of $0.01 each. On the same day, the Company issued 1,709,650 Series B-2 convertible preferred shares for consideration of $18.85 each, for gross cash proceeds of $32,230.

The holders of the convertible preferred shares have the following rights and preferences:

Voting Rights

The holders of convertible preferred shares are entitled to vote, together with the holders of ordinary shares, on all matters submitted to shareholders for a vote, except the election of ordinary share directors and except as required by law. In addition, a number of actions require consent of at least two thirds of the holders of the convertible preferred shares which must include holders of at least 55% of the then outstanding Series B convertible preferred shares. Each preferred shareholder is entitled to the number of votes equal to the number of ordinary shares into which each preferred share is convertible as of the day of the vote (being 1:1, subject to any adjustments arising).

Liquidation Preferences

In the event that the Company liquidates, dissolves or winds up, whether voluntarily or involuntarily, or sells all or substantially all of its assets, or sells the Company or a controlling interest in the Company or if certain events deemed to be a liquidation occur, then the holders of the Series B convertible preferred shares shall be entitled to receive in preference to the holders of the Series A convertible preferred shares and the ordinary shares; and the holders of the Series A convertible preferred shares shall be entitled to receive in preference of the ordinary shares, an amount per share equal to the original purchase price for the convertible preferred shares, plus any dividends, if declared but unpaid thereon. Following all preferential payments to holders of the

convertible preferred shares as required, any remaining undistributed assets shall be shared ratably to the holders of the ordinary shares and the convertible preferred shares with the latter's share number being determined on an "as-if-converted" basis, until such time as the preferred shareholders have received, in total, an amount equal to three times the applicable original purchase price. Thereafter, any remaining net assets available are distributed ratably to the ordinary shareholders only.

Dividends

The holders of the convertible preferred shares are entitled to receive, if declared by the Board, non-cumulative dividends at the rate of 8% of the original purchase price per annum. Such dividends shall only be payable when and if declared and are not cumulative.

The holders of convertible preferred shares have liquidation and dividend rights in preference to the holders of ordinary shares. No dividends on the ordinary shares shall be declared and paid unless dividends on the convertible preferred shares have been declared and paid. Through March 31, 2018, the Company has not declared any dividends.

Redemption Rights

The convertible preferred shares are not redeemable at the option of the holder.

Conversion Rights

Each preferred share is convertible at any time at the option of the shareholder into fully paid ordinary shares. The conversion ratio is fixed at 1:1, except in the event that the Company issues additional shares of stock below the purchase price of the preferred share, share splits and combinations, dividends and distributions whereby, the conversion price may be adjusted, with certain exceptions. In the event of a liquidation, dissolution, winding up or deemed liquidation event, the conversion rights will be terminated at the close of business on the last day preceding the date fixed for payment of liquidation amounts to the holders of convertible preferred shares.

Mandatory Conversion

All outstanding shares will automatically convert into ordinary shares, based on the then effective applicable conversion price upon the closing of the sale of ordinary shares to the public in a firm-commitment underwritten public offering on the New York Stock Exchange, the Nasdaq Global Market, Nasdaq Global Select Market or such other market or exchange as approved by the Board pursuant to an effective registration statement under the Securities Act of 1933, as amended, in which the per share price is at least $51.84 and the gross cash proceeds to the company are at least forty million dollars ($40,000); or the affirmative election (in writing) of the holders of at least two thirds of the convertible preferred shares, which must include holders of at least 55% of the then outstanding Series B convertible preferred shares.

(9) 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 stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock awards. The types of share-based awards, including share purchase 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 Equity Incentive 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 will become effective immediately on the execution and delivery of the underwriting agreement related to the IPO. Once the 2018 Plan is effective, no further grants will be made under the 2015 Equity Incentive Plan.

The 2018 Plan authorizes the Company to grant up to 1,018,459 ordinary shares in the form of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, performance stock awards, performance cash awards and other stock awards. The types of share-based awards, including share purchase rights amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors.

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 vest 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 $333 and $333 for the years ended December 31, 2016 and December 31, 2017, respectively. Total unamortized compensation expense related to restricted ordinary shares was $925 and $592 as of December 31, 2016 and December 31, 2017, respectively, expected to be recognized over a weighted average period of 2.88 years and 1.88 years as of December 31, 2016 and December 31, 2017, respectively.

The Company recorded an expense of $82 and $82 for the restricted ordinary shares for the periods ended March 31, 2017 and March 31, 2018, respectively. Total unamortized compensation expense related to restricted ordinary shares was $843 and $510 as of March 31, 2017 and March 31, 2018, respectively, expected to be recognized over a weighted average period of 2.63 years and 1.63 years as of March 31, 2017 and March 31, 2018, respectively.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

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, 2015	413,110	$ 3.14
Granted	—	
Vested	(120,490)	$ 3.14
Forfeited	—	
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	(25,819)	$ 3.14
Forfeited	—	
Unvested at March 31, 2018 (unaudited)	163,523	$ 3.14

Share Options

Unless specified otherwise in an individual option agreement, share options granted under the 2015 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, 2016 and December 31, 2017 and for the period ended March 31, 2018 was estimated using the Black-Scholes option-pricing model. The inputs for the Black-Scholes model require management's significant assumptions. The ordinary share price was determined by the Board of Directors. In the absence of market data for the Company's ordinary shares, the Board of Directors considered various factors in estimating the fair value of the ordinary shares at the time of grant which include but are not limited to the ordinary shares valuation performed by a third-party independent valuation firm, the Company's performance and future economic outlook, the potential financing available to the Company, and the valuation of ordinary shares of similar companies in the industry. Following the closing of this offering, the fair value of ordinary shares will be determined based on the quoted market price of the Company's shares. The risk-free interest rate was based on a normalized estimate of the 7-year U.S. treasury yield. The expected life was based on the simplified method in accordance with the Securities and Exchange Commission ("SEC") Staff Accounting Bulletin Nos. 107 and 110 as the Company's shares are not publicly traded. The expected volatility was estimated based on historical volatility information of reasonably comparable guideline public companies that are publicly available. Expected dividend yield is based on the fact that the Company has never paid cash dividends 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.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

The Company granted 49,330 and 198,798 stock options to employees and directors during the years ended December 31, 2016 and December 31, 2017, respectively. There were 49,330 and 228,809 unvested employee options outstanding as of December 31, 2016 and December 31, 2017, respectively. Total expense recognized related to the employee stock options was $15 and $59 for the years ended December 31, 2016 and December 31, 2017, respectively. Total unamortized compensation expense related to employee stock options was $75 and $396 as of December 31, 2016 and December 31, 2017, respectively which is expected to be recognized over a remaining average vesting period of 3.54 years and 3.51 years as of December 31, 2016 and December 31, 2017, respectively.

The Company granted 14,320 stock options to employees and directors for the three month period ended March 31, 2017. The Company awarded 74,152 stock options to employees during the period ended March 31, 2018 under the 2018 Plan. These options will be granted and priced upon execution of the underwriting agreement related to the IPO. There were 58,801 and 221,553 unvested employee options outstanding as of March 31, 2017 and March 31, 2018, respectively. Total expense recognized related to the employee stock options was $7 and $67 for the periods ended March 31, 2017 and March 31, 2018, respectively. Total unamortized compensation expense related to employee stock options was $95 and $1,132 as of March 31, 2017 and March 31, 2018, respectively, which is expected to be recognized over a remaining average vesting period of 3.43 years and 3.27 years as of March 31, 2017 and March 31, 2018, respectively.

The assumptions that the Company used to determine the grant date fair value of employee and director options granted were as follows, presented on a weighted average basis:

	Year Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
			(unaudited)	
Volatility	60%	60%	60%	60%
Expected term in years	6.25	6.25	6.25	6.25
Dividend rate	0%	0%	0%	0%
Risk-free interest rate	2.00%	1.63%	1.63%	1.63%
Share price	$3.14	$3.36	$ 3.30	—
Fair value of option on grant date	$1.80	$1.91	$ 1.88	—

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

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 at December 31, 2015	—			
Granted	49,330	$ 3.14		
Exercised	—			
Forfeited	—			
Options outstanding at December 31, 2016	49,330	$ 3.14	8.51	
Granted	198,798	$ 3.36	9.67	
Exercised	—			
Forfeited	—			
Options outstanding at December 31, 2017	248,128	$ 3.31	9.44	
Granted	—			
Exercised	—			
Forfeited	—			
Options Outstanding March 31, 2018	248,128	$ 3.31	9.19	3,856
Vested at March 31, 2018 (unaudited)	26,575			417
Exercisable at March 31, 2018 (unaudited)	26,575	$ 3.17	8.33	417

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 at March 31, 2018.

The Company's share-based compensation expense was classified in the consolidated statements of operations and comprehensive loss as follows:

	Year Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
			(unaudited)	
Research and development expense	$115	$139	$ 31	$ 71
General and administrative expense	233	253	58	78

There was a total of $1,000 and $988 unamortized share-based compensation expense for restricted ordinary shares and options as of December 31, 2016 and December 31, 2017, respectively, which is expected to be recognized over a remaining average vesting period of 2.93 years and 2.53 years as of December 31, 2016 and December 31, 2017, respectively.

There was a total of $938 and $1,642 unamortized share-based compensation expense for restricted ordinary shares and options as of March 31, 2017 and March 31, 2018, respectively, which is expected to be recognized over a remaining average vesting period of 2.71 years and 2.32 years as of March 31, 2017 and March 31, 2018, respectively.

(10) Income Taxes

During the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018 (unaudited), the Company recorded no income tax benefits for the net operating losses incurred in each year or interim period due to its uncertainty of realizing a benefit from those items.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

The provision for income taxes consists of the following components:

	Year ended December 31, 2016	Year ended December 31, 2017
Current		
U.S.	$ 113	$ 444
Ireland	—	—
Total current	113	444
Deferred		
U.S.	—	—
Ireland	—	—
Total deferred	—	—
Income tax provision	$ 113	$ 444

Income taxes have been based on the following components of income (loss) before provision for income taxes:

	Year ended December 31, 2016	Year ended December 31, 2017
U.S.	$ (50)	$ 875
Ireland	(13,414)	(30,281)
Total	$ (13,464)	$ (29,406)

The Irish federal statutory rate is reconciled to the effective tax rate as follows:

	Year ended December 31, 2016	
Statutory rate	12.50%	$(1,683)
Impact of U.S. tax rate	0.10%	(48)
Impact of valuation allowance	(12.69%)	1,709
Other, net	(0.75%)	135
Effective tax rate	(0.84%)	113

	Year ended December 31, 2017	
Statutory rate	12.50%	$(3,676)
Impact of U.S. tax rate	(0.79%)	232
Impact of valuation allowance	(13.43%)	3,949
Research and development tax credit	0.75%	(220)
Other, net	(0.54%)	159
Effective tax rate	(1.51%)	$ 444

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

The significant components of the Company's deferred tax assets and liabilities are as follows:

	December 31, 2016	December 31, 2017
Deferred tax assets		
Share-based compensation	$ 1	$ 3
Depreciation	—	6
Net operating loss carryforwards	1,706	5,409
Other	2	240
Valuation allowance	(1,709)	(5,658)
Total deferred tax assets	—	—
Deferred tax liabilities	—	—
Total deferred tax liabilities	—	—
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 which result in tax benefits of approximately $1,706 and $5,409 for the years ended December 31, 2016 and December 31, 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.

A reconciliation of the beginning and ending amount of gross unrecognized tax benefits is as follows:

	2016	2017
Balance at January 1	$ —	$ —
Additions	—	30
Balance at December 31	$ —	$ 30

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.

(11) Commitments and Contingencies

Operating Leases

In March 2018, the Company entered into an operating lease agreement for office space in Chicago for a period of five years that commences in June 2018. Annual lease payments are $258, subject to certain escalations, with a renewal option to extend the lease for an additional five years. Under the terms of the lease, the Company provided a security deposit in the form of a letter of credit for the benefit of the landlord in the amount of $120 which will be reduced incrementally over the term of the lease. The letter of credit outstanding is collateralized with a certificate of deposit.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

In April 2017, the Company entered into an operating lease agreement for office space in Connecticut for a period of five years that commenced in July 2017. Annual lease payments are $131, subject to certain escalations, with a renewal option to extend the lease for an additional three years. Under the terms of the lease, the Company provided a security deposit of $17 to the landlord, which is included in other assets in the accompanying consolidated balance sheets.

In December 2016, the Company entered into an operating lease agreement for office space in Dublin that commenced on December 1, 2016 and expires on December 1, 2026. The lease requires annual payments of $375 over the ten-year term with a renewal option to extend the lease for an additional five years. Under the terms of the lease, the Company provided a security deposit of $356 to the landlord, which is included in other assets in the accompanying consolidated balance sheets. The lease is subject to a review in December 2022.

The following table summarizes the future minimum payments due under the operating leases as of March 31, 2018:

Year Ending March 31,	
2019	$ 698
2020	750
2021	759
2022	769
2023	710
Thereafter	1,353
	$5,039

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 development 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 $3,017 to the supplier to acquire equipment which will be used solely to manufacture product for the Company. This payment will be offset against the price of the product to be supplied under a future supply agreement. $1,578, $599 and $616 remained outstanding to the supplier as of December 31, 2016, December 31, 2017 and March 31, 2018, respectively.

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.

ITERUM THERAPEUTICS PLC

Notes to Consolidated Financial Statements
(In thousands, except share and per share data)

Under the terms of their respective employment agreements, each of the named 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 delivery to the Company of a satisfactory release of claims, and subject to the named executive officer's compliance with non-competition and non-solicitation restrictive covenants for one year following the termination date.

(12) Subsequent Events

The Company has evaluated subsequent events through March 9, 2018, the date the annual consolidated financial statements were issued. For the issuance of the financial statements for the three months ended March 31, 2018, the unaudited interim period presented herein, such evaluation has been performed through May 4, 2018.

Debt

On April 27, 2018, the Company's subsidiaries, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited, entered into a Loan and Security Agreement with Silicon Valley Bank (SVB) and made an initial draw of $15,000 on closing. A second draw of up to $15,000 will be available to the Company through October 31, 2019, upon satisfaction of either (i) the achievement by the Company of both 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 trial.

The initial draw will require monthly amortization payments commencing on November 1, 2019; however this will extend to April 1, 2020 if the second draw is funded. Interest will accrue 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 4.2% final interest payment, will be due and payable on March 1, 2022. Voluntary prepayments will be permitted at any time, subject to a prepayment fee of 3% in the first year, 2% in the second year, and 1% thereafter.

In connection with the initial $15,000 draw, the Company issued to SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B convertible preferred shares at an exercise price of $18.85 per share. On the funding date of the second term loan, each of SVB and LSF will be automatically entitled to purchase additional ordinary shares in an aggregate amount equal to 2.5% of the second term loan divided by the applicable exercise price.

Reverse Share Split

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 stock awards, warrants and per share amounts have been retroactively adjusted to reflect this Reverse Share Split and Renominalisation for all periods presented.

Table of Contents

5,333,333 Ordinary Shares

Prospectus

, 2018

Leerink Partners **RBC Capital Markets**

Guggenheim Securities

Needham & Company

Through and including , 2018 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. ***Other Expenses of Issuance and Distribution.***

The following table sets forth all costs and expenses, other than underwriting discounts and commissions, payable by Iterum Therapeutics plc (the "Registrant") in connection with the sale of the ordinary shares being registered. All amounts shown are estimates except for the Securities and Exchange Commission ("SEC") registration fee, the Financial Industry Regulatory Authority, Inc. ("FINRA") filing fee and the initial listing fee.

	Amount
SEC registration fee	$ 12,218
FINRA filing fee	15,220
Nasdaq initial listing fee	125,000
Legal fees and expenses	2,000,000
Accounting fees and expenses	240,000
Printing and engraving expenses	175,000
Transfer agent and registrar fees and expenses	290,000
Miscellaneous expenses	142,562
Total	$3,000,000

Item 14. ***Indemnification of Directors and Officers.***

To the fullest extent permitted by Irish law, our Articles of Association (which are substantially in the form attached as an exhibit to this registration statement) will confer an indemnity on our directors and officers. However, this indemnity is limited by the Irish Companies Act, which prescribe that an advance commitment to indemnify only permits a company to pay the costs or discharge the liability of a director or corporate secretary where judgment is given in favor of the director or corporate secretary in any civil or criminal action in respect of such costs or liability, or where an Irish court grants relief because the director or corporate secretary acted honestly and reasonably and ought fairly to be excused. Any provision whereby an Irish company seeks to commit in advance to indemnify its directors or corporate secretary over and above the limitations imposed by the Irish Companies Act will be void under Irish law, whether contained in its articles of association or any contract between the company and the director or corporate secretary. This restriction does not apply to our executives who are not directors, the corporate secretary or other persons who would be considered "officers" within the meaning of that term under the Irish Companies Act.

Our Articles of Association will also contain indemnification and expense advancement provisions for persons who are not directors or our corporate secretary.

We are permitted under our Articles of Association and the Irish Companies Act to purchase directors' and officers' liability insurance, as well as other types of insurance, for our directors, officers, employees and agents.

Additionally, we have entered into agreements to indemnify our directors and executive officers to the maximum extent allowed under Irish law.

In addition, one of our Delaware subsidiaries has entered into indemnification agreements with each of our directors and executive officers whereby we have agreed to indemnify our directors and officers to the fullest extent permitted by law, including indemnification against expenses and liabilities incurred in legal proceedings to which the director or officer was, or is threatened to be made, a party by reason of the fact that such director or officer is or was a director, officer, employee or agent of Iterum, provided that such director or officer acted in

good faith and in a manner that the director or officer reasonably believed to be in, or not opposed to, the best interest of Iterum. At present, there is no pending litigation or proceeding involving a director or officer of Iterum regarding which indemnification is sought, nor is the registrant aware of any threatened litigation that may result in claims for indemnification.

As of the time of the closing of this offering, we will have in place insurance policies that indemnify our directors and officers against various liabilities arising under the Securities Act and the Securities Exchange Act of 1934, as amended, that might be incurred by any director or officer in his or her capacity as such.

The underwriters are obligated, under certain circumstances, pursuant to the underwriting agreement to be filed as Exhibit 1.1 hereto, to indemnify us and our officers and directors against liabilities under the Securities Act.

Item 15. ***Recent Sales of Unregistered Securities.***

The following sets forth information regarding all unregistered securities issued and sold by the Registrant since January 1, 2015:

(1) In October 2015, we sold an aggregate of 413,110 of our ordinary shares to six accredited investors at a price per share of $0.001571 per share, for an aggregate purchase price of $649.

(2) From March 2016 to date, we have granted stock options under our 2015 Equity Incentive Plan to purchase an aggregate of 248,128 ordinary shares with exercise prices ranging between $3.14 and $4.40 per share to 31 employees, directors and consultants, all of which remain outstanding.

(3) In November 2015, we issued an aggregate of 1,514,320 of our Series A preferred shares to 12 accredited investors at a purchase price of $15.71 per share, for an aggregate purchase price of $20.7 million plus the receipt of a license to certain intellectual property.

(4) In December 2016, we issued an aggregate of 1,518,137 of our Series A preferred shares to 12 accredited investors at a purchase price of $15.71 per share, for an aggregate purchase price $20.9 million plus the receipt of a license to certain intellectual property.

(5) In May 2017, we issued an aggregate of 2,654,206 of our Series B-1 preferred shares to 17 accredited investors at a purchase price of $17.28 per share, for an aggregate purchase price $45.9 million.

(6) In February 2018, we issued an aggregate of 1,709,650 of our Series B-2 preferred shares to 17 accredited investors at a purchase price of $18.85 per share, for an aggregate purchase price of $32.2 million.

(7) In April 2018, we issued warrants to purchase an aggregate of 19,890 of our Series B-2 preferred shares to two accredited investors at an exercise price of $18.85 per share, for an aggregate exercise price of $374,927.

The offers, sales and issuances of the securities described in paragraphs 1, 3, 4, 5, 6 and 7 above 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.

The offers, sales and issuances of the securities described in paragraphs 2 above were exempt from registration under compensatory benefit plans and contracts relating to compensation as provided under either (a) Rule 701 promulgated under the Securities Act or (b) under Section 4(a)(2) of the Securities Act (or Regulation D promulgated thereunder).

The Registrant did not pay or give, directly or indirectly, any commission or other remuneration, including the underwriting discounts and commissions, in connection with any of the issuances of securities listed above. The recipients of the securities in each of these transactions represented their intentions to acquire the securities for investment only and not with a view to or for sale in connection with any distribution thereof, and appropriate legends were placed upon the share certificates issued in these transactions. All recipients had adequate access, through their employment or other relationship with us or through other access to information provided by the Registrant, to information about it. The sales of these securities were made without any general solicitation or advertising.

Table of Contents

Item 16. ***Exhibits and Financial Statement Schedules*****.**

(a) Exhibits.

Exhibit Index

Exhibit No.	Description of Document
1.1#	Form of Underwriting Agreement.
3.1	Constitution, as currently in effect.
3.2	Form of Constitution (including the Articles of Association), to be effective upon the closing of this offering.
4.1#	Form of Ordinary Share Certificate of Registrant.
5.1	Opinion of A&L Goodbody.
10.1†#	License Agreement by and among Registrant, Iterum Therapeutics International Limited and Pfizer Inc. dated as of November 18, 2015.
10.2#	Amended and Restated Investor Rights Agreement by and between Registrant and certain of its shareholders dated May 18, 2017.
10.3+#	2015 Equity Incentive Plan.
10.4+#	Forms of U.S. Stock Option Agreement, Stock Option Grant Notice and Notice of Exercise under the 2015 Equity Incentive Plan.
10.5+#	Forms of Irish Stock Option Agreement, Stock Option Grant Notice and Notice of Exercise under the 2015 Equity Incentive Plan.
10.6+	2018 Equity Incentive Plan.
10.7+#	Forms of U.S. Stock Option Terms and Conditions and Stock Option Grant Notice under the 2018 Equity Incentive Plan.
10.8+#	Forms of International Stock Option Terms and Conditions and Stock Option Grant Notice under the 2018 Equity Incentive Plan.
10.9+#	Form of Restricted Share Unit Award Agreement under the 2018 Equity Incentive Plan.
10.10#	Form of Indemnity Agreement by and between the Registrant and its directors and officers.
10.11#	Form of Indemnity Agreement by and between Iterum Therapeutics US Limited and its directors and officers.
10.12+#	Employment Terms by and between Iterum Therapeutics US Limited and Corey N. Fishman dated November 18, 2015.
10.13+#	Amendment to Employment Agreement by and between Iterum Therapeutics US Limited and Corey N. Fishman dated May 2, 2018.
10.14+#	Employment Terms by and between Iterum Therapeutics US Limited and Michael W. Dunne dated November 18, 2015.
10.15+#	Employment Terms by and between Iterum Therapeutics US Limited and Judith M. Matthews dated November 18, 2015.
10.16+#	Amendment to Employment Agreement by and between Iterum Therapeutics US Limited and Judith M. Matthews dated May 2, 2018.
10.17+#	Employment Terms by and between Iterum Therapeutics US Limited and Jeffrey Schaffnit dated February 9, 2018.

Exhibit No.	Description of Document
10.18+	Non-Employee Director Compensation Policy.
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.
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.
10.21#	Warrant to Subscribe for Shares, issued to Silicon Valley Bank, dated April 27, 2018.
10.22#	Warrant to Subscribe for Shares, issued to Life Sciences Fund II LLC, dated April 27, 2018.
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.
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.
21.1#	Subsidiaries of the Registrant.
23.1	Consent of KPMG, Independent Registered Public Accounting Firm.
23.2	Consent of A&L Goodbody (reference is made to Exhibit 5.1).
24.1#	Power of Attorney (reference is made to the signature page hereto).

+ 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.
# Previously filed.

(b) Financial Statement Schedules.

No financial statement schedules are provided because the information called for is not required or is shown either in the financial statements or the notes thereto.

Item 17. ***Undertakings.***

The Registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant has duly caused this Amendment No. 2 to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Chicago, State of Illinois, on the 16th day of May, 2018.

ITERUM THERAPEUTICS PLC

/s/ Corey N. Fishman
Corey N. Fishman
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act, this Amendment No. 2 to the Registration Statement has been signed by the following persons 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)	May 16, 2018
/s/ Judith M. Matthews Judith M. Matthews	Chief Financial Officer (Principal Financial and Accounting Officer)	May 16, 2018
* Paul R. Edick	Chairman of the Board of Directors	May 16, 2018
* Brenton K. Ahrens	Director	May 16, 2018
* Mark Chin	Director	May 16, 2018
* James I. Healy, M.D., Ph.D.	Director	May 16, 2018
* Patrick J. Heron	Director	May 16, 2018
* Ronald M. Hunt	Director	May 16, 2018
* David G. Kelly	Director	May 16, 2018
* Shahzad Malik, M.D.	Director	May 16, 2018

SIGNATURE	TITLE	DATE
*	Director	May 16, 2018
Robert Hopfner, Ph.D.		

* By: /s/ Corey N. Fishman
Corey N. Fishman
Attorney-in-fact

COMPANIES ACT 2014

A PUBLIC COMPANY LIMITED BY SHARES

CONSTITUTION

OF

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY

A & L Goodbody
Solicitors

COMPANIES ACT 2014

A PUBLIC COMPANY LIMITED BY SHARES

MEMORANDUM OF ASSOCIATION

OF

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY

1. The name of the Company is Iterum Therapeutics public limited company.

2. The Company is a public limited company for the purposes of Part 17 of the Companies Act 2014.

3. The objects for which the Company is established are:

   3.1. To carry on the business of a holding company and to coordinate the administration, finances and activities of any subsidiary companies or associated companies, to do all lawful acts and things whatsoever that are necessary or convenient in carrying on the business of such a holding company and in particular to carry on, in all its branches, the business of a management services company, to act as managers and to direct or coordinate the management of other companies or of the business, property and estates of any company or person and to undertake and carry out all such services in connection therewith as may be deemed necessary or appropriate by the Company's board of directors and to exercise its powers as a shareholder of other companies.

   3.2. To carry on the business of a pharmaceuticals company and to research, develop, design, manufacture, produce, supply, buy, sell, distribute, import, export, provide, promote and otherwise deal in pharmaceuticals, active pharmaceutical ingredients and dosage pharmaceuticals and other devices or products of a pharmaceutical, medicinal or healthcare character and to hold intellectual property rights and to do all things usually done by persons carrying on the above mentioned activities or any of them or likely to be required in connection with any such activities.

   3.3. To invest in pharmaceutical and related assets, including, amongst other items, investments in pharmaceutical companies, products, businesses, divisions, technologies, devices, sales force and other marketing capabilities, development projects and related activities, licences, intellectual and similar property rights, premises and equipment, royalty rights and all other assets needed to operate a pharmaceuticals business.

   3.4. To establish, maintain and operate laboratories for the purposes of carrying on chemical, physical and other research in medicine, chemistry, industry or other unrelated or related fields.

   3.5. To invest (including long-term investments in, and acquisitions of, the shares or other securities or ownership interests in other companies) any monies of the Company in such investments and in such manner as may from time to time be determined, and to hold,

sell or deal with such investments and generally to purchase, take on lease or in exchange or otherwise acquire any real and personal property and rights or privileges.

3.6. To develop and turn to account any land acquired by the Company or in which it is interested and in particular by laying out and preparing the same for building purposes, constructing, altering, pulling down, decorating, maintaining, fitting up and improving buildings and conveniences, and by planting, paving, draining, farming, cultivating, letting on building lease or building agreement and by advancing money to and entering into contracts and arrangements of all kinds with builders, tenants and others.

3.7. To acquire and hold shares and stocks of any class or description, debentures, debenture stocks, bonds, bills, mortgages, obligations, investments, partnership interests, limited partnership interests, trust interests, membership interests and other securities or ownership interests of all descriptions and of any kind issued or guaranteed by any company or undertaking of whatever nature and wheresoever constituted or carrying on business or issued or guaranteed by any government, state, dominion, colony, sovereign ruler, commissioners, trust, public, municipal, local or other authority or body of whatever nature and wheresoever situated and investments, securities and property of all descriptions and of any kind, including real and chattel real estates, mortgages, reversions, assurance policies, contingencies and choses in action.

3.8. To remunerate by cash payments or allotment of shares or securities or other ownership interests (including rights to acquire shares or securities or other ownership interests) of the Company credited as fully paid up or otherwise any person or company for services rendered or to be rendered to the Company or any parent or subsidiary body corporate whether in the conduct or management of its business, or in placing or assisting to place or guaranteeing the placing of any of the shares of the Company's capital, or any debentures or other securities of the Company or in or about the formation or promotion of the Company.

3.9. To purchase for investment property of any tenure and any interest therein, and to make advances upon the security of land or other similar property or any interest therein.

3.10. To acquire by purchase, exchange, lease, fee, farm grant or otherwise, either for an estate in fee simple or for any less estate or other estate or interest, whether immediate or reversionary and whether vested or contingent, any lands, tenements or hereditaments of any tenure, whether subject or not to any charges or encumbrances, and to hold, farm, work and manage and to let, sublet, mortgage or charge land and buildings of any kind, reversions, interests, annuities, life policies, and any other property real or personal, movable or immovable, either absolutely or conditionally, and either subject or not to any mortgage, charge, ground rent or other rents or encumbrances.

3.11. To erect or secure the erection of buildings or other structures of any kind with a view of occupying or letting them or otherwise utilising them and to enter into any contracts or leases and to grant any licences necessary to effect the same.

3.12. To maintain and improve any lands, tenements or hereditaments acquired by the Company or in which the Company is interested, in particular by decorating, maintaining, furnishing, fitting up and improving houses, shops, flats, maisonettes and other buildings and structures and to enter into contracts and arrangements of all kinds with tenants and others.

3.13. To sell, exchange, mortgage (with or without power of sale), assign, turn to account or otherwise dispose of and generally deal with the whole or any part of the property, shares, stocks, securities, estates, rights or undertakings of the Company, real property, chattels real or personal, movable or immovable, either in whole or in part.

3.14. To take part in the management, supervision, or control of the business or operations of any company or undertaking, and for that purpose to appoint and remunerate any directors, accountants, or other experts or agents to act as consultants, supervisors and agents of other companies or undertakings and to provide managerial, advisory, technical, design, purchasing and selling services and any other services deemed appropriate by the Company.

3.15. To make, draw, accept, endorse, negotiate, issue, execute, discount and otherwise deal with bills of exchange, promissory notes, letters of credit, circular notes, and other negotiable or non-negotiable or transferable or non-transferrable instruments.

3.16. To redeem, purchase, or otherwise acquire in any manner permitted by law any shares in the Company's capital or other securities or ownership interests of any kind issued by the Company.

3.17. To guarantee, support or secure whether by personal covenant or by mortgaging or charging all or any part of the undertaking, property and assets (present and future) and uncalled capital of the Company or by both such methods, or by any other method whatsoever, the performance of the obligations of, and the repayment or payment of the principal amounts of and the premiums, interest, dividends and other amounts due on or with respect to any security of any person, firm or company, including any company which is for the time being the Company's holding company (as defined by section 8 of the Companies Act 2014) or subsidiary (as defined by section 7 of the Companies Act 2014) or another subsidiary as defined by the said section of the Company's holding company (as defined by section 8 of the Companies Act 2014) or otherwise associated with the Company in business notwithstanding the fact that the Company may not receive any consideration, advantage or benefit, direct or indirect from entering into such guarantee or other arrangement or transaction contemplated herein.

3.18. To lend the funds of the Company with or without security and at interest or free of interest.

3.19. To raise or borrow or secure the payment of money, including by the issue of bonds, debentures or debenture stock, perpetual or redeemable, or by mortgage, charge, lien or pledge upon the whole or any part of the undertaking, property, assets or rights of the Company, present or future, including its uncalled capital and generally in any other manner as the directors shall from time to time determine and to enter into or issue interest and currency hedging and swap agreements, forward rate agreements, interest and currency futures or options and other forms of financial instruments, and to purchase, redeem or pay off any of the foregoing and to guarantee any or all of the liabilities of the Company, any other company or any other person, and any debentures, debenture stock or other securities may be issued at a discount, premium or otherwise, and with any special privileges as to redemption, surrender, transfer, drawings, allotments of shares, attending and voting at general meetings of the Company, appointment of directors and otherwise.

3.20. To accumulate capital for any of the purposes of the Company, and to appropriate any of the Company's assets to specific purposes, either conditionally or unconditionally, and to admit any class or section of those who have any dealings with the Company to any share in the profits thereof or in the profits of any particular branch of the Company's business or to any other special rights, privileges, advantages or benefits.

3.21. To reduce the share capital of the Company in any manner permitted by law.

3.22. To make gifts or grant bonuses to officers or other persons who are or have been in the employment of the Company and to allow any such persons to have the use and

enjoyment of such property, chattels or other assets belonging to the Company upon such terms as the Company shall think fit.

3.23. To establish and maintain or procure the establishment and maintenance of any pension or superannuation fund (whether contributory or otherwise) for the benefit of and to give or procure the giving of donations, gratuities, pensions, annuities, allowances, emoluments or charitable aid to any persons who are or were at any time in the employment or service of the Company or any of its predecessors in business, or of any company which is a subsidiary of the Company or who may be or have been directors or officers of the Company, or of any such other company as aforesaid, or any persons in whose welfare the Company or any such other company as aforesaid may be interested and the wives, husbands, widows, widowers, families, relatives or dependants of any such persons, and to make payments towards insurance and assurance and to form and contribute to provident and benefit funds for the benefit of any such persons and to remunerate any person, firm or company rendering services to the Company or of any company which is a subsidiary of the Company, whether by cash payment, gratuities, pensions, annuities, allowances, emoluments or by the allotment of shares or securities of the Company credited as paid up in full or in part or otherwise.

3.24. To employ experts to investigate and examine into the conditions, prospects, value, character and circumstances of any business concerns, undertakings, assets, property or rights.

3.25. To insure the life of any person who may, in the opinion of the Company, be of value to the Company, as having or holding for the Company interests, goodwill, or influence or otherwise and to pay the premiums on such insurance.

3.26. To distribute either upon a distribution of assets or division of profits among the Members of the Company in kind any property of the Company, and in particular any shares, debentures or securities of other companies belonging to the Company or of which the Company may have the power of disposing.

3.27. To give, whether directly or indirectly, and whether by means of a loan, guarantee, the provision of security or otherwise, any financial assistance for the purpose of or in connection with a purchase or subscription made or to be made by any person of or for any shares in the Company, or, where the Company is a subsidiary company, in its holding company.

3.28. To do and carry out all or any of the foregoing or following objects in any part of the world and either as principals, agents, contractors, trustees or otherwise, and either by or through agents, trustees or otherwise and either alone or in partnership or in conjunction with any other company, firm or person, provided that nothing herein contained shall empower the Company to carry on the business of insurance.

3.29. To apply for, purchase or otherwise acquire any patents, brevets d'invention, licences, trademarks, trade names, copyrights, industrial designs, know-how, concessions and other forms of intellectual property rights and the like conferring any exclusive or non-exclusive or limited or contingent rights to use, or any secret or other information as to any invention or process of the Company, or the acquisition of which may seem calculated directly or indirectly to benefit the Company, and to use, exercise, develop, or grant licences in respect of, or otherwise turn to account the property, rights or information so acquired.

3.30. To enter into partnership or into any arrangement for sharing profits, union of interests, co-operation, joint venture, reciprocal concession or otherwise with any person or company.

3.31. To acquire and undertake the whole or any part of the undertaking, business, property and liabilities of any person or company.

3.32. To adopt such means of making known the Company and its products and services as may seem expedient.

3.33. To acquire and carry on any business carried on by a subsidiary or a holding company of the Company or another subsidiary of a holding company of the Company.

3.34. To promote any company or companies for the purpose of acquiring all or any of the property and liabilities of this Company or for any other purpose which may seem directly or indirectly calculated to benefit this Company.

3.35. To amalgamate with, merge with or otherwise become part of or associated with any other company or association in any manner permitted by law.

3.36. To make voluntary dispositions of all or any part of the property and rights of the Company and to make gifts thereof or gratuitous payments either for no consideration or for a consideration less than the market value of such property or rights or the amount of cash payment or by all or any such methods.

3.37. To receive voluntary dispositions of all or any part of the undertakings, properties, assets or rights of any other corporation and to receive gifts thereof or gratuitous payments either for no consideration or for a consideration less than the market value of such property or rights or the amount of cash payment or by all or any such methods.

3.38. To do and carry out all such other things, except the issuing of policies of insurance, as may be deemed by the Company capable of being carried on in connection with the above objects or any of them or calculated to enhance the value of or render profitable any of the Company's undertakings, properties, assets or rights.

And it is hereby declared that (i) the word "company" in this clause, except where used in reference to this Company, shall be deemed to include any person, partnership, limited partnership, limited liability partnership, limited liability company, other corporate body, trust or other body of persons whether incorporated or not incorporated and whether domiciled in Ireland or elsewhere and that the objects of the Company as specified in each of the foregoing paragraphs of this clause shall be separate and distinct objects and shall not be in anyway limited or restricted by reference to or inference from the terms of any other paragraph or the name of the Company and (ii) any phrase introduced by the terms "including", "include", "in particular" or any similar expression shall be construed as illustrative and shall not limit the sense of the words preceding those terms.

4. The liability of each Member is limited to the amount from time to time unpaid on such Member's Shares.

5. The share capital of the Company is US$523,915.62 divided into 44,557,606 ordinary shares of US$0.01 each (the "**Ordinary Shares**") and 3,032,463 Series A preferred shares of US$0.01 each (the "**Series A Preferred Shares**") and 2,654,215 Series B-1 preferred shares of US$0.01 each (the "**Series B-1 Preferred Shares**") and 2,147,278 Series B-2 preferred shares of US$0.01 each (the "**Series B-2 Preferred Shares**").

6. The shares forming the capital, increased or reduced, may be increased or reduced and be divided into such classes and issued with any special rights, privileges and conditions or with such qualifications as regards preference, dividend, capital, voting or other special incidents, and be held upon such terms as may be attached thereto or as may from time to time be provided by the original or any substituted or amended Articles of Association and regulations of the Company for the time being, but so that where shares are issued with any preferential or special rights

attached thereto such rights shall not be alterable otherwise than pursuant to the provisions of the Company's Articles of Association for the time being.

7. Capitalised terms that are not defined in this Memorandum of Association bear the same meaning as those given in the Articles of Association of the Company.

COMPANIES ACT 2014

A PUBLIC COMPANY LIMITED BY SHARES

ARTICLES OF ASSOCIATION

OF

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY

PRELIMINARY

1. **Preliminary, Definitions and Interpretation:**

1.1. In this Constitution, unless the context otherwise requires:

Act means the Companies Act 2014;

Acquisition means any (**A**) sale, scheme of arrangement, consolidation or merger of the Company to, with or into any other corporation or other entity or person, or any other corporate reorganization, other than any such sale, scheme of arrangement, consolidation, merger or reorganization in which the shares of the Company immediately prior to such sale, scheme of arrangement, consolidation, merger or reorganization, continue to represent at least a majority of the voting power of the surviving entity (or, if the surviving entity is a wholly owned subsidiary, its parent) immediately after such sale, scheme of arrangement, consolidation, merger or reorganization, (provided that, for the purpose of Regulation 37, all Ordinary Shares issuable upon exercise of options outstanding immediately prior to such consolidation or merger or upon conversion of Convertible Securities outstanding immediately prior to such sale, scheme of arrangement, consolidation or merger shall be deemed to be outstanding immediately prior to such sale, scheme of arrangement, consolidation or merger and, if applicable, converted or exchanged in such sale, scheme of arrangement, consolidation or merger on the same terms as the actual outstanding shares are converted or exchanged); or (**B)** transaction or series of related transactions to which the Company is a party in which in excess of fifty percent (50%) of the Company's voting power is transferred**;** provided that an Acquisition shall not include any transaction or series of transactions principally for bona fide equity financing purposes in which cash is received by the Company or any successor or indebtedness of the Company is cancelled or converted or a combination thereof;

Affiliates means with respect to any specified Investor, any other Investor who directly or indirectly, controls, is controlled by or is under common control with such Investor, including, without limitation, (a) any general partner, managing member, officer or director of such Investor, or any venture capital fund now or hereafter existing which is controlled by one or more general partners or managing members of, or shares the same management company with, such Investor or (b) with respect to any corporation, any parent corporation or wholly-owned subsidiary of such corporation, or any direct or indirect wholly-owned subsidiary of the ultimate parent entity of such corporation;

Asset Transfer means the completion of a sale, lease, exclusive license, assignment or other disposition of all or substantially all of the business and assets of the Company;

Additional Ordinary Shares means Ordinary Shares issued by the Company or deemed to be issued (including Ordinary Shares subsequently reacquired or cancelled by the Company), other than:

(a) Ordinary Shares issued upon conversion of the Series Preferred Shares;

(b) Ordinary Shares issued as a dividend or distribution on the Series Preferred Shares;

(c) Ordinary Shares or Convertible Securities issued after the Original Issue Date to employees, officers or directors of, or consultants or advisors to, the Company or any subsidiary pursuant to share purchase or share option plans or other arrangements that are approved by the Board, including at least one Series Preferred Director;

(d) Ordinary Shares or Convertible Securities issued pursuant to a firmly underwritten public offering pursuant to an effective registration statement under the United States Securities Act of 1933, as amended, or pursuant to an equivalent filing on any other market or exchange approved by the Board and the Requisite Super Majority;

(e) Ordinary Shares or Convertible Securities issued for consideration other than cash pursuant to a sale, scheme of arrangement, merger, consolidation, acquisition, strategic alliance or similar business combination approved by a Requisite Super Majority;

(f) Ordinary Shares or Convertible Securities issued pursuant to any equipment loan or leasing arrangement, real property leasing arrangement or debt financing from a bank or similar financial or lending institution approved by the Board, including at least one Series Preferred Director;

(g) Ordinary Shares or Convertible Securities issued in connection with Strategic Transactions involving the Company and other entities approved by the Board, including at least one Series Preferred Director, where "Strategic Transactions" means research and development partnerships, licensing, corporate partnering, collaborative arrangements or similar transactions; and

(h) Ordinary Shares or Convertible Securities that the Requisite Super Majority elect in writing to exclude from the definition of "Additional Ordinary Shares";

Adoption Date means the date of adoption of this Constitution.

Board means the board of directors or, as the context may require, any duly authorised committee of the board of directors;

committee means a committee established by the directors which may consist in whole or in part of members of the board of directors of the Company;

Convertible Securities means (i) Series A Preferred Shares; (ii) Series B-1 Preferred Shares; (iii) Series B-2 Preferred Shares; or (iv) other shares, options, warrants, purchase rights or other securities exercisable for or convertible into Additional Ordinary Shares;

Defaulting Investor means a "Defaulting Investor" as defined in the Series B Share Purchase Agreement;

director means a director for the time being of the Company or a director present at a meeting of the board of directors and includes any person occupying the position of director by whatever name called, and **directors** means all of such persons;

Group Company means the Company or the Company's holding company or a subsidiary of the Company or its holding company;

Investor means the holder of (i) any Series A Preferred Shares issued pursuant to the terms of the Series A Share Purchase Agreement; (ii) any Series B-1 Preferred Shares or Series B-2 Preferred Shares issued pursuant to the terms of the Series B Share Purchase Agreement; and/or (iii) any Ordinary Shares into which such Series A Preferred Shares, Series B-1 Preferred Shares or Series B-2 Preferred Shares have converted;

Ireland means Ireland excluding Northern Ireland;

Liquidation Event means any Asset Transfer, Acquisition, liquidation, dissolution, or winding up of the Company, whether voluntary or involuntary;

Requisite Super Majority means holders of at least two thirds of the outstanding Series Preferred Shares, which must include holders of at least 55% of the then outstanding Series B Preferred Shares;

Series A Director means any Director appointed by the holders of Series A Preferred Shares in accordance with Regulation 14.2.1;

Series A Original Issue Price means US$1.00 (as adjusted for any share dividends, combinations, splits, recapitalizations and the like with respect to the Series A Preferred Shares after the date of adoption hereof);

Series A Share Purchase Agreement means the Series A Preferred Share purchase agreement by and between the Company and holders of Series A Preferred Shares dated as of 18 November 2015 (as amended and restated by the Amendment and Restatement Agreement between the Company and holders of Series A Preferred Shares dated 9 December 2016);

Series B Director means any Director appointed by the holders of Series B Preferred Shares in accordance with Regulation 14.2.2;

Series B-1 Original Issue Price means US$1.10 (as adjusted for any share dividends, combinations, splits, recapitalizations and the like with respect to the Series B-1 Preferred Shares after the date of adoption hereof); and

Series B-2 Original Issue Price means US$1.20 (as adjusted for any share dividends, combinations, splits, recapitalizations and the like with respect to the Series B-2 Preferred Shares after the date of adoption hereof);

Series B Preferred Shares means shares of the Company's Series B-1 Preferred Shares or shares of the Company's Series B-2 Preferred Shares;

Series B Share Purchase Agreement means the Series B-1 and B-2 Preferred Share purchase agreement by and between the Company and holders of Series B Preferred Shares dated as of 18 May 2017 (as amended and restated by Amendment No. 1 to the Series B-1 and B-2 Share Purchase Agreement between the Company and holders of Series B Preferred Shares dated 16 February 2018);

Series Preferred Director means any Series A Director or Series B Director;

Series Preferred Shares means the (i) Series A Preferred Shares, (ii) Series B-1 Preferred Shares and (iii) Series B-2 Preferred Shares;

Shareholders Agreements means the amended and restated investor rights agreement, amended and restated voting agreement, and amended and restated right of first refusal and co-sale agreement entered into by the Company, the Investors, and others specified therein as of 18 May 2017;

the seal means the common seal of the Company; and

the register means the register of members to be kept as required by the Act and **registered address** means the address of a member as entered in the register.

1.2. With the exceptions of sections 83 (*variation of company capital*) and 84 (*reduction in company capital*) of the Act, which provisions shall be modified and shall apply to the Company as provided for in this Constitution, no "optional provisions" as defined by section 1007(2) of the Act, shall bind the Company and its members.

1.3. Unless the contrary is clearly stated, references to the Act or to any other enactment (including any subordinate legislation) or any section or provision thereof shall mean the Act or such enactment, subordinate legislation, section or provision (as the case may be), as the same may be consolidated, amended, extended, modified, supplemented or re-enacted (whether before or after the date hereof) from time to time and may be for the time being in force.

1.4. Unless specifically defined in this Constitution or the context otherwise requires, words or expressions contained in this Constitution and not specifically defined herein shall bear the same meanings as in the Act, but excluding any statutory modification thereof not in force when this Constitution became binding on the Company and the members.

1.5. Reference to any document includes that document as amended or supplemented from time to time.

1.6. Unless the context otherwise requires, expressions in this Constitution referring to writing shall be construed, unless the contrary intention appears, as including references to printing, lithography, photography and to writing in electronic form and any other modes of representing or reproducing words in a visible form, and expressions in this Constitution referring to execution of any document shall include any mode of execution whether under seal or under hand.

1.7. Unless the context otherwise requires, words importing the singular include the plural and vice versa, words importing the masculine include the feminine, and words importing persons include corporations.

1.8. Headings are inserted for convenience only and do not affect the construction or interpretation of this Constitution.

1.9. Unless the context otherwise requires, reference to Regulations and to paragraphs in this Constitution are to the Regulations, and paragraphs of the Regulations, of this Constitution.

2. **Share Capital:**

The share capital of the Company is US$523,915.62 divided into 44,557,606 ordinary shares of US$0.01 each (the "**Ordinary Shares**") and 3,032,463 Series A preferred shares of US$0.01 each (the "**Series A Preferred Shares**") and 2,654,215 Series B-1 preferred shares of US$0.01 each (the "**Series B-1 Preferred Shares**") and 2,147,278 Series B-2 preferred shares of US$0.01 each (the "**Series B-2 Preferred Shares**").

3. **Company Seal:** Without prejudice to the provisions of the Act in relation to the use of the seal of a company, any registered person authorised by the board of directors of the Company in accordance with the applicable provisions of the Act will be entitled to use the seal of the Company and may sign or countersign an instrument to which the seal is affixed, and an alternate who is not also a director will also be entitled to sign or countersign an instrument to which the seal is affixed, as if he were the director who appointed him. The seal shall be used only by the authority of the directors or of a committee of directors authorised by the directors in that behalf.

4. **Official Seal:** The Company may have for use in any place abroad an official seal which shall resemble the seal of the Company with the addition on its face of the name of every place abroad where it is to be used.

5. **Authority to Allot Shares:**

5.1. Subject to the Regulations set out in this Constitution, the directors are, for the purposes of section 1021 of the Companies Act, generally and unconditionally authorised to exercise all powers of the Company to allot and issue relevant securities (as defined by the said section 1021) up to the amount of the Company's authorised but unissued share capital as at the Adoption Date and to allot and issue any shares in the capital of the Company acquired by or on behalf of the Company pursuant to the provisions of the Companies Act and held as treasury shares and, unless it is renewed or a longer period of time is allowed under applicable law, this authority shall expire five years from the Adoption Date.

5.2. Subject to the Regulations set out in this Constitution, the directors are hereby empowered pursuant to sections 1022 and 1023(3) of the Companies Act to allot equity securities within the meaning of the said section 1023 for cash pursuant to the authority conferred by Regulation 5.1 as if section 1022 of the Companies Act did not apply to any such allotment.

5.3. The Company may before the expiry of the authorities conferred by Regulations 5.1 and/or 5.2 make an offer or agreement which would or might require relevant securities (as defined in section 1021 of the Companies Act) and/or equity securities (as defined in section 1023 of the Companies Act), as the case may be, to be allotted after such expiry and the Board may allot relevant securities and/or equity securities in pursuance of such an offer or agreement as if the authorities conferred by Regulations 5.1 and/or 5.2 had not expired.

5.4. **Right of First Refusal**: Each Investor (with its Affiliates) that owns not less than 1,000,000 Series Preferred Shares (as adjusted for share splits and combinations) (a "***Major Investor***") shall have a right of first refusal to subscribe for its *pro rata* share of all Equity Securities, as defined below, that the Company may, from time to time, propose to sell and issue after the date of adoption hereof, other than those shares excluded from the definition of Additional Ordinary Shares. Each Investor's *pro rata* share is equal to the ratio of (a) the number of the Company's Ordinary Shares (including all Ordinary Shares issuable or issued upon conversion of the Series Preferred Shares or upon the exercise of outstanding warrants or options) of which such Investor is deemed to be a holder immediately prior to the issuance of such Equity Securities to (b) the total number of the Company's outstanding Ordinary Shares (including all Ordinary Shares issued or issuable upon conversion of the Series Preferred Shares or upon the exercise of any outstanding warrants or options) immediately prior to the issuance of the Equity Securities. The term "***Equity Securities***" for the purposes of this Regulation 5.4 shall mean (i) any Ordinary Shares, Series Preferred Shares or other security of the Company, (ii) any security convertible into or exercisable or exchangeable for, with or without consideration, any Ordinary Shares, Series Preferred Shares or other equity security

(including any option to purchase such a convertible security), (iii) any equity security carrying any warrant or right to subscribe to or purchase any Ordinary Shares, Series Preferred Shares or other security or (iv) any such warrant or right.

5.4.1. **Exercise of Rights.** If the Company proposes to issue any Equity Securities, it shall give each Major Investor written notice of its intention, describing the Equity Securities, the price and the terms and conditions upon which the Company proposes to issue the same. Each Major Investor shall have 20 days from the giving of such notice to agree to subscribe for its *pro rata* share of the Equity Securities for the price and upon the terms and conditions specified in the notice by giving written notice to the Company and stating therein the quantity of Equity Securities to be subscribed for. Notwithstanding the foregoing, the Company shall not be required to offer or issue such Equity Securities to any Major Investor who would cause the Company to be in violation of applicable securities laws by virtue of such offer or sale.

5.4.2. **Issuance of Equity Securities to Other Persons**. If not all of the Major Investors elect to subscribe for their full *pro rata* share of the Equity Securities, then the Company shall promptly notify in writing the Major Investors who do so elect and shall offer such Major Investors the right to subscribe for such unsubscribed shares on a *pro rata* basis. The Major Investors shall have 10 days after receipt of such notice to notify the Company of its election to subscribe for all or a portion thereof of the unsubscribed shares. The Company shall have 90 days thereafter to sell the Equity Securities in respect of which the Major Investor's rights were not exercised, at a price and upon general terms and conditions not materially more favorable to the purchasers thereof than specified in the Company's notice to the Major Investors pursuant to Regulation 5.4.1. If the Company has not issued such Equity Securities within 90 days of the notice provided pursuant to Regulation 5.4.1, the Company shall not thereafter issue any Equity Securities, without first offering such securities to the Major Investors in the manner provided above.

5.4.3. **Sale Without Notice.** In lieu of giving notice to the Major Investors prior to the issuance of Equity Securities as provided in Regulation 5.4, the Company may elect to give notice to the Major Investors within 30 days after the issuance of Equity Securities. Such notice shall describe the type, price and terms of the Equity Securities. Each Major Investor shall have 20 days from the date of receipt of such notice to elect to subscribe for up to the number of shares that would, if purchased by such Major Investor, maintain such Major Investor's *pro rata* share (as set forth in Regulation 5.4) of the Company's Equity Securities. The closing of such issuance shall occur within 60 days of the date of notice to the Major Investors.

5.5. Shares and any other securities of the Company may only be allotted by the directors or a duly authorised committee thereof and the directors (or any duly authorised committee) may allot, grant options over, issue or otherwise dispose of shares or other securities to such persons, on such terms and conditions, and at such times as they may determine in their absolute discretion subject to the Regulations set out in this Constitution.

5.6. The directors or any duly authorised committee thereof may execute and do all such documents, acts and things as in their opinion are necessary or desirable in order to give effect to the authority conferred by this Regulation.

5.7. For the purposes of this Regulation, **shares** includes a right to subscribe for shares or to convert securities into shares and **securities** has the meaning given to such term in Section 64(1) of the Act.

6. **Dividend Rights:**

6.1. The holders of the Series Preferred Shares, in preference to the holders of the Ordinary Shares, shall be entitled to receive, but only out of funds that are legally available therefor, (as determined in accordance with the Act), cash dividends at the rate of 8% of the Applicable Original Issue Price (as defined below) per annum on each outstanding share of the Series Preferred Shares. Such dividends shall be payable only when, as and if declared by the Board and shall be non-cumulative.

6.2. The "***Applicable Original Issue Price***" means the Series A Original Issue Price, the Series B-1 Original Issue Price, and/or the Series B-2 Original Issue Price, as applicable with respect to the relevant series.

6.3. So long as any shares of the Series Preferred Shares are outstanding, the Company shall not pay or declare any dividend (whether in cash or property), or make any other distribution or return of capital on the Ordinary Shares, or purchase, redeem or otherwise acquire for value any Ordinary Shares, until all dividends as set forth in Regulation 6.1 above on the Series Preferred Shares shall have been paid or declared and set apart, except for:

6.3.1. acquisitions of Ordinary Shares by the Company pursuant to agreements that permit the Company to repurchase such shares at no more than cost upon termination of services to the Company (as approved by the Board);

6.3.2. acquisitions of Ordinary Shares in exercise of the Company's right of first refusal to acquire such shares (whether pursuant to an agreement approved by the Board and/or pursuant to this Constitution); or

6.3.3. distributions to holders of Ordinary Shares in accordance with Regulation 37.

6.4. No dividends shall be paid on any share of Ordinary Shares, unless at the same time the Company shall pay an additional dividend on all outstanding shares of Series Preferred Shares in a per share amount equal (on an as-if-converted to Ordinary Shares basis) to or greater than the amount paid or set aside for each share of Ordinary Shares. The Company in general meeting may declare dividends on Ordinary Shares, but no dividend shall exceed the amount recommended by the directors. Subject to this Regulation 6, the directors may from time to time pay to the members of the Company such interim dividends as appear to the directors to be justified by the profits of the Company.

7. **Voting Rights**

7.1. **General Rights.** Each holder of shares of the Series Preferred Shares shall be entitled to the number of votes equal to the number of Ordinary Shares into which such shares of Series Preferred Shares could be converted (pursuant to Regulation 8) immediately after the close of business on the record date fixed for such meeting or the effective date of such written consent and shall have voting rights and powers equal to the voting rights and powers of the Ordinary Shares and shall be entitled to notice of any shareholders' meeting in accordance with the Constitution of the Company. Except as otherwise provided herein or as required by law, the Series Preferred Shares shall vote together with the Ordinary Shares at any annual or special meeting of the shareholders and not as a separate class, and may act by written consent in the same manner as the Ordinary Shares.

7.2. **Separate Vote of Series Preferred Shares.** For so long as any shares of the Series Preferred Shares (as adjusted for any share dividends, combinations, splits, recapitalizations and the like with respect to such shares after the date of adoption

hereof) remain outstanding, in addition to any other vote or consent required herein or by law, the vote or written consent of the Requisite Super Majority shall be necessary for effecting or validating the following actions, which results in the following (and the constitution or bylaws or equivalent of any subsidiary of the Company shall include equivalent provisions in favour of the holders of Series Preferred Shares):

7.2.1. Any amendment, alteration, or repeal of any provision of the Constitution of the Company, including, without limitation, any amendment that alters or changes the voting or other powers, preferences, or other rights, privileges or restrictions of the Series Preferred Shares (whether by merger, recapitalization, reclassification, amendment or otherwise);

7.2.2. Any increase or decrease in the authorized number of shares of Ordinary Shares, Series Preferred Shares or any other class of shares;

7.2.3. Any authorization or any designation, whether by merger, reclassification, amendment or otherwise, or any other action resulting in the creation of any new class or series of shares or any other securities convertible into a new class or series of shares of the Company;

7.2.4. Any redemption, repurchase, payment or declaration of dividends or other distributions or return of capital with respect to Ordinary Shares, Series Preferred Shares or any other class of shares (except for acquisitions of Ordinary Shares by the Company referred to in Regulation 6.3.1 hereof);

7.2.5. Any agreement by the Company or its shareholders regarding or any other action resulting in an Asset Transfer or Acquisition;

7.2.6. Any incurrence of bank indebtedness of US$500,000 or more individually or in the aggregate with all other bank indebtedness of the Company (other than payables incurred in the ordinary course of business);

7.2.7. Any voluntary dissolution or liquidation of the Company;

7.2.8. Any increase or decrease in the authorized number of members of the Company's Board; or

7.2.9. Any increase in the number of shares available for issuance under any existing equity incentive plan or the creation of any new equity incentive plan.

Notwithstanding the foregoing or anything contained in this Constitution to the contrary, if any action approved by the Requisite Super Majority pursuant to Regulation 7.2 treats any outstanding series of the Series Preferred adversely and in a manner that is materially different than how the other outstanding series of Series Preferred are treated (such series, the "**Targeted Series**"), then such action shall also require the approval of the holders of a majority of the outstanding shares of the Targeted Series, provided that the creation or authorisation of one or more new series of preferred stock that is senior or pari passu to the Targeted Series with respect to its rights, preferences or privileges shall not be deemed to adversely affect the Targeted Series.

7.3. Variation of Class Rights

7.3.1. **Variation of Class Rights or Nominal Value**. For the purposes of each of Regulations 7.3.1 and 7.3.2, the variation or abrogation of the rights attaching to a class of shares ("**Relevant Class**") includes each of the following: (i) any variation or abrogation of class rights of the Relevant Class within the meaning of the Act, including any variation in the number of

authorised Series Preferred Shares; and (ii) any variation in the nominal (par) value of the Relevant Class ("**Class Rights**"). Subject to Regulation 7.3.2 below, the Class Rights attaching to the Ordinary Shares and the Series Preferred Shares shall not be varied or abrogated without:

(1) the consent in writing of (i) a Requisite Super Majority (in the case of a variation or abrogation of the Class Rights attaching to the Series Preferred Shares) or (ii) the holders of in excess of 50% in nominal value of the issued Ordinary Shares (in the case of a variation or abrogation of the Class Rights attaching to the Ordinary Shares other than any variation in the authorised number of Ordinary Shares, with respect to which Regulation 7.3.3 shall govern); or

(2) the sanction of (i) a resolution passed at a separate general meeting of the holders of the Series Preferred Shares passed by holders of the Series Preferred Shares representing a Requisite Super Majority (in the case of a variation or abrogation of the Class Rights attaching to the Series Preferred Shares) or (ii) an ordinary resolution passed at a separate general meeting of the holders of the Ordinary Shares (in the case of a variation or abrogation of the Class Rights attaching to the Ordinary Shares other than any variation in the authorised number of Ordinary Shares, with respect to which Regulation 7.3.3 shall govern).

7.3.2. **Variation of Class Rights for Future Fund Raising Round**. Notwithstanding anything to the contrary in Regulation 7.3.1, the approval of a new class of shares having superior capital, dividend, voting, anti-dilution, liquidation or other rights to any currently existing class of shares, without any other changes to the Class Rights of such existing class of shares, shall not in and of itself be deemed a variation or an abrogation of the Class Rights attaching to such existing class of shares for purposes of Regulation 7.3.1.

7.3.3. **Authorised Shares**. The number of authorised Ordinary Shares may be increased or decreased (but not below the number of Ordinary Shares, as applicable, then in issue) by (in addition to any vote of the holders of Series Preferred Shares that may be required by the terms of this Constitution) the affirmative vote of the holders of shares in the capital of the Company representing a majority of the votes represented by all issued shares in the capital of the Company entitled to vote and at all times in accordance with the Act.

8. **Conversion Rights.**

8.1. The holders of the Series Preferred Shares shall have the following rights with respect to the conversion of the Series Preferred Shares into Ordinary Shares (the "***Conversion Rights***"):

8.1.1. **Optional Conversion.** Subject to and in compliance with the provisions of this Regulation 8, any of the Series Preferred Shares may, at the option of the holder, be converted at any time into fully paid Ordinary Shares. The number of Ordinary Shares to which a holder of Series Preferred Shares shall be entitled upon conversion shall be the product obtained by multiplying the "Applicable Conversion Rate" then in effect (determined as provided in Regulation 8.1.2) by the number of shares of Series Preferred Shares being converted.

8.1.2. **Applicable Conversion Rate.** The conversion rate in effect at any time for conversion of any series of Series Preferred Shares (the "***Applicable Conversion Rate***") shall be the quotient obtained by dividing the Applicable Original Issue Price of such series of Series Preferred Shares by the "Applicable Conversion Price," calculated as provided in Regulation 8.1.3.

8.1.3. **Applicable Conversion Price.** The "***Applicable Conversion Price***" for the relevant series of Series Preferred Shares shall initially be equal to (a) the Series A Original Issue Price, in the case of shares of Series A Preferred Shares, (b) the Series B-1 Original Issue Price, in the case of shares of Series B-1 Preferred Shares, and (c) the Series B-2 Original Issue Price, in the case of shares of Series B-2 Preferred Shares. Such initial Applicable Conversion Price shall be adjusted from time to time in accordance with this Regulation 8. All references to the Applicable Conversion Price herein shall mean the Applicable Conversion Price as so adjusted.

8.1.4. **Mechanics of Optional Conversion.** Each holder of the Series Preferred Shares who desires to convert the same into Ordinary Shares pursuant to this Regulation 8 shall surrender the certificate or certificates therefor, duly endorsed, at the registered office of the Company or at the office of any transfer agent for the Series Preferred Shares, and shall give written notice to the Company at such office that such holder elects to convert the same. Such notice shall state the number of shares of the Series Preferred Shares being converted. Thereupon, the Company shall promptly issue and deliver at such office to such holder a certificate or certificates for the number of Ordinary Shares to which such holder is entitled and shall promptly pay (i) in cash or, to the extent sufficient funds are not then legally available therefor (as determined in accordance with the Act), in Ordinary Shares (at the Ordinary Shares' fair market value determined in good faith by the Board as of the date of such conversion), any declared and unpaid dividends on the shares of the Series Preferred Shares being converted and (ii) in cash (at the Ordinary Shares' fair market value determined in good faith by the Board as of the date of conversion) the value of any fractional share of Ordinary Shares otherwise issuable to any holder of Series Preferred Shares. Such conversion shall be deemed to have been made at the close of business on the date of such surrender of the certificates representing the shares of Series Preferred Shares to be converted, and the person entitled to receive the Ordinary Shares issuable upon such conversion shall be treated for all purposes as the record holder of such Ordinary Shares on such date.

8.1.5. **Adjustment for Share Splits and Combinations.** If at any time or from time to time on or after the date that the first share of the Series B Preferred Shares is issued (the "***Original Issue Date***") the Company effects a subdivision of the outstanding Ordinary Shares, the Applicable Conversion Price in effect immediately before that subdivision shall be proportionately decreased. Conversely, if at any time or from time to time after the Original Issue Date the Company combines the outstanding Ordinary Shares into a smaller number of shares, the Applicable Conversion Price in effect immediately before the combination shall be proportionately increased. Any adjustment under this Regulation 8.1.5 shall become effective at the close of business on the date the subdivision or combination becomes effective.

8.1.6. **Adjustment for Ordinary Shares Dividends and Distributions.** If at any time or from time to time on or after the Original Issue Date the Company pays to holders of Ordinary Shares a dividend or other

distribution in additional Ordinary Shares (without a corresponding dividend or other distribution on the Series Preferred Shares), the Applicable Conversion Price then in effect shall be decreased as of the time of such issuance, as provided below:

(a) The Applicable Conversion Price shall be adjusted by multiplying the Applicable Conversion Price then in effect by a fraction equal to:

(i) the numerator of which is the total number of Ordinary Shares issued and outstanding immediately prior to the time of such issuance, and

(ii) the denominator of which is the total number of Ordinary Shares issued and outstanding immediately prior to the time of such issuance plus the number of Ordinary Shares issuable in payment of such dividend or distribution;

(b) If the Company fixes a record date to determine which holders of Ordinary Shares are entitled to receive such dividend or other distribution, the Applicable Conversion Price shall be fixed as of the close of business on such record date and the number of Ordinary Shares shall be calculated immediately prior to the close of business on such record date; and

(c) If such record date is fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the Applicable Conversion Price shall be recomputed accordingly as of the close of business on such record date and thereafter the Applicable Conversion Price shall be adjusted pursuant to this Regulation 8.1.6 to reflect the actual payment of such dividend or distribution.

8.1.7. **Adjustment for Reclassification, Exchange, Substitution, Reorganization, Merger or Consolidation.** If at any time or from time to time on or after the Original Issue Date the Ordinary Shares issuable upon the conversion of the Series Preferred Shares are changed into the same or a different number of shares of any class or classes of shares, whether by recapitalization, reclassification, merger, consolidation or otherwise (other than an Acquisition or a subdivision or combination of shares or share dividend provided for elsewhere in this Regulation 8), in any such event each share of the Series Preferred Shares shall thereafter be convertible in lieu of the Ordinary Shares into which it was convertible prior to such event into the kind and amount of securities, cash or other property that a holder of the number of Ordinary Shares of the Company issuable upon conversion of one share of the Series Preferred Shares immediately prior to such recapitalization, reclassification, merger, consolidation or other transaction would have been entitled to receive pursuant to such transaction, all subject to further adjustment as provided herein or with respect to such other securities or property by the terms thereof. In any such case, appropriate adjustment shall be made in the application of the provisions of this Regulation 8 with respect to the rights of the holders of the Series Preferred Shares after the capital reorganization to the end that the provisions of this Regulation 8 (including adjustment of the Applicable Conversion Price then in effect and the number of shares issuable upon conversion of the Series Preferred Shares) shall be applicable after that event and be as nearly equivalent as practicable.

8.1.8. **Sale of Shares Below Applicable Conversion Price.**

(a) If at any time or from time to time on or after the Original Issue Date the Company issues or sells, or is deemed by the express provisions of this Regulation 8.1.8 to have issued or sold, Additional Ordinary Shares, other than as provided in Regulations 8.1.5, 8.1.6 or 8.1.7 above, for an Effective Price (as defined below) less than the then effective Applicable Conversion Price (a "***Qualifying Dilutive Issuance***"), then and in each such case, the then existing Applicable Conversion Price shall be reduced, as of the opening of business on the date of such issue or sale, to a price determined by multiplying the Applicable Conversion Price in effect immediately prior to such issuance or sale by a fraction:

(i) the numerator of which shall be (A) the number of Ordinary Shares deemed outstanding (as determined below) immediately prior to such issue or sale, plus (B) the number of Ordinary Shares that the Aggregate Consideration (as defined below) received or deemed received by the Company for the total number of Additional Ordinary Shares so issued would purchase at such then-existing Applicable Conversion Price, and

(ii) the denominator of which shall be the number of Ordinary Shares deemed outstanding (as determined below) immediately prior to such issue or sale plus the total number of Additional Ordinary Shares so issued.

For the purposes of the preceding sentence, the number of Ordinary Shares deemed to be outstanding as of a given date shall be the sum of (x) the number of Ordinary Shares outstanding, (y) the number of Ordinary Shares into which the then outstanding shares of Series Preferred Shares could be converted if fully converted on the day immediately preceding the given date, and (z) the number of Ordinary Shares that are issuable upon the exercise or conversion of all other rights, options and convertible securities outstanding on the day immediately preceding the given date.

(b) [Intentionally Blank].

(c) For the purpose of making any adjustment required under this Regulation 8.1.8, the aggregate consideration received by the Company for any issue or sale of securities (the "***Aggregate Consideration***") shall be defined as: (x) to the extent it consists of cash, the gross amount of cash received by the Company before deduction of any underwriting or similar commissions, compensation or concessions paid or allowed by the Company in connection with such issue or sale and without deduction of any expenses payable by the Company, (y) to the extent it consists of property other than cash, the fair market value of that property as determined in good faith by the Board, and (z) if Additional Ordinary Shares, Convertible Securities or rights or options to purchase either Additional Ordinary Shares or Convertible Securities are issued or sold together with other shares or securities or other assets of the Company for a consideration that covers both, the portion of the consideration so received that may be reasonably determined in good faith by the Board to be allocable to such Additional Ordinary Shares, Convertible Securities or rights or options.

(d) For the purpose of the adjustment required under this Regulation 8.1.8, if the Company issues or sells (x) preferred shares or other shares, options, warrants, purchase rights or other securities exercisable for or convertible into, Additional Ordinary Shares (such convertible shares or securities being herein referred to as "***Convertible Securities***") or (y) rights or options for the purchase of Additional Ordinary Shares or Convertible Securities and if the Effective Price of such Additional Ordinary Shares is less than the Applicable Conversion Price, in each case the Company shall be deemed to have issued at the time of the issuance of such rights or options or Convertible Securities the maximum number of Additional Ordinary Shares issuable upon exercise or conversion thereof and to have received as consideration for the issuance of such shares an amount equal to the total amount of the consideration, if any, received by the Company for the issuance of such rights or options or Convertible Securities plus:

(i) in the case of such rights or options, the minimum amounts of consideration, if any, payable to the Company upon the exercise of such rights or options; and

(ii) in the case of Convertible Securities, the minimum amounts of consideration, if any, payable to the Company upon the conversion thereof (other than by cancellation of liabilities or obligations evidenced by such Convertible Securities); *provided* that if the minimum amounts of such consideration cannot be ascertained, but are a function of antidilution or similar protective clauses, the Company shall be deemed to have received the minimum amounts of consideration without reference to such clauses.

(iii) If the minimum amount of consideration payable to the Company upon the exercise or conversion of rights, options or Convertible Securities is reduced over time or on the occurrence or non-occurrence of specified events other than by reason of antidilution adjustments, the Effective Price shall be recalculated using the figure to which such minimum amount of consideration is reduced; *provided further,* that if the minimum amount of consideration payable to the Company upon the exercise or conversion of such rights, options or Convertible Securities is subsequently increased, the Effective Price shall be again recalculated using the increased minimum amount of consideration payable to the Company upon the exercise or conversion of such rights, options or Convertible Securities.

(iv) No further adjustment of the Applicable Conversion Price, as adjusted upon the issuance of such rights, options or Convertible Securities, shall be made as a result of the actual issuance of Additional Ordinary Shares or the exercise of any such rights or options or the conversion of any such Convertible Securities. If any such rights or options or the conversion privilege represented by any such Convertible Securities shall expire without having been exercised, the Applicable Conversion Price as adjusted upon the issuance of such rights, options or Convertible Securities shall be readjusted to the Applicable Conversion Price that would have

been in effect had an adjustment been made on the basis that the only Additional Ordinary Shares so issued were the Additional Ordinary Shares, if any, actually issued or sold on the exercise of such rights or options or rights of conversion of such Convertible Securities, and such Additional Ordinary Shares, if any, were issued or sold for the consideration actually received by the Company upon such exercise, plus the consideration, if any, actually received by the Company for the granting of all such rights or options, whether or not exercised, plus the consideration received for issuing or selling the Convertible Securities actually converted, plus the consideration, if any, actually received by the Company (other than by cancellation of liabilities or obligations evidenced by such Convertible Securities) on the conversion of such Convertible Securities, *provided* that such readjustment shall not apply to prior conversions of the Series Preferred Shares.

References to Ordinary Shares in the subsections of this clause (d) above shall mean all Ordinary Shares issued by the Company or deemed to be issued pursuant to this Regulation 8.1.8. The "***Effective Price***" of Additional Ordinary Shares shall mean the quotient determined by dividing the total number of Additional Ordinary Shares issued or sold, or deemed to have been issued or sold by the Company under this Regulation 8.1.8, into the Aggregate Consideration received, or deemed to have been received by the Company for such issue under this Regulation 8.1.8, for such Additional Ordinary Shares. In the event that the number of shares of Additional Ordinary Shares or the Effective Price cannot be ascertained at the time of issuance, such Additional Ordinary Shares shall be deemed issued immediately upon the occurrence of the first event that makes such number of shares or the Effective Price, as applicable, ascertainable.

(e) In the event that the Company issues or sells, or is deemed to have issued or sold, Additional Ordinary Shares in a Qualifying Dilutive Issuance (the "**First Dilutive Issuance**"), then in the event that the Company issues or sells, or is deemed to have issued or sold, Additional Ordinary Shares in a Qualifying Dilutive Issuance other than the First Dilutive Issuance as a part of the same transaction or series of related transactions as the First Dilutive Issuance (a "**Subsequent Dilutive Issuance**"), then and in each such case upon a Subsequent Dilutive Issuance the Applicable Conversion Price shall be reduced to the Applicable Conversion Price that would have been in effect had the First Dilutive Issuance and each Subsequent Dilutive Issuance all occurred on the closing date of the First Dilutive Issuance.

8.1.9. **Certificate of Adjustment.** In each case of an adjustment or readjustment of the Applicable Conversion Price for the number of Ordinary Shares or other securities issuable upon conversion of the Series Preferred Shares, if the Series Preferred Shares is then convertible pursuant to this Regulation 8, the Company, at its expense, shall compute such adjustment or readjustment in accordance with the provisions hereof and shall, upon request, prepare a certificate showing such adjustment or readjustment, and shall mail such certificate, by first class mail, postage prepaid, to each registered holder of the Series Preferred Shares so requesting at the

holder's address as shown in the Company's books. The certificate shall set forth such adjustment or readjustment, showing in detail the facts upon which such adjustment or readjustment is based, including a statement of (i) the consideration received or deemed to be received by the Company for any Additional Ordinary Shares issued or sold or deemed to have been issued or sold, (ii) the Applicable Conversion Price at the time in effect, (iii) the number of Additional Ordinary Shares and (iv) the type and amount, if any, of other property that at the time would be received upon conversion of the Series Preferred Shares. Failure to request or provide such notice shall have no effect on any such adjustment.

8.1.10. **Notices of Record Date.** Upon (i) any taking by the Company of a record of the holders of any class of securities for the purpose of determining the holders thereof who are entitled to receive any dividend or other distribution, or (ii) any Acquisition or other capital reorganization of the Company, any reclassification or recapitalization of the shares of the Company, any merger or consolidation of the Company with or into any other corporation, or any Asset Transfer, or any voluntary or involuntary dissolution, liquidation or winding up of the Company, the Company shall mail to each holder of the Series Preferred Shares at least ten (10) days prior to (x) the record date, if any, specified therein; or (y) if no record date is specified, the date upon which such action is to take effect (or, in either case, such shorter period approved by the Requisite Super Majority) a notice specifying (A) the date on which any such record is to be taken for the purpose of such dividend or distribution and a description of such dividend or distribution, (B) the date on which any such Acquisition, reorganization, reclassification, transfer, consolidation, merger, Asset Transfer, dissolution, liquidation or winding up is expected to become effective, and (C) the date, if any, that is to be fixed as to when the holders of record of Ordinary Shares (or other securities) shall be entitled to exchange their Ordinary Shares (or other securities) for securities or other property deliverable upon such Acquisition, reorganization, reclassification, transfer, consolidation, merger, Asset Transfer, dissolution, liquidation or winding up.

8.1.11. **Automatic Conversion.**

(a) Each share of the Series Preferred Shares shall automatically be converted into Ordinary Shares, based on the then-effective Applicable Conversion Price, (A) at any time upon the affirmative election (in writing) of the Requisite Super Majority, or (B) immediately upon the closing of a firmly underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, or pursuant to an equivalent filing on any other market or exchange approved by the Board, covering the offer and sale of Ordinary Shares for the account of the Company in which (i) the per share price is at least US$3.30 or foreign exchange equivalent (as adjusted for any share dividends, combinations, splits, recapitalizations and the like with respect to such shares after the date of adoption hereof), (ii) the gross cash proceeds to the Company (before underwriting discounts, commissions and fees) are at least US$40,000,000 or foreign exchange equivalent and (iii) the Company's shares have been listed for trading on the New York Stock Exchange, NASDAQ Global Select Market, NASDAQ Global Market or such other market or exchange as approved by the Board. Upon such automatic conversion, any declared and unpaid dividends shall be paid in accordance with the provisions of Regulation 8.1.4.

(b) Upon the occurrence of either of the events specified in Regulation 8.1.11(a) above, the outstanding shares of the Series Preferred Shares shall be converted automatically without any further action by the holders of such shares and whether or not the certificates representing such shares are surrendered to the Company or its transfer agent; *provided, however*, that the Company shall not be obligated to issue certificates evidencing the Ordinary Shares issuable upon such conversion unless the certificates evidencing such shares of the Series Preferred Shares are either delivered to the Company or its transfer agent as provided below, or the holder notifies the Company or its transfer agent that such certificates have been lost, stolen or destroyed and executes an agreement satisfactory to the Company to indemnify the Company from any loss incurred by it in connection with such certificates. Upon the occurrence of such automatic conversion of the Series Preferred Shares, the holders of Series Preferred Shares shall surrender the certificates representing such shares at the office of the Company or any transfer agent for the Series Preferred Shares. Thereupon, there shall be issued and delivered to such holder promptly at such office and in its name as shown on such surrendered certificate or certificates, a certificate or certificates for the number of Ordinary Shares into which the shares of the Series Preferred Shares surrendered were convertible on the date on which such automatic conversion occurred, and any declared and unpaid dividends shall be paid in accordance with the provisions of Regulation 8.1.4.

8.1.12. **Special Mandatory Conversion.**

(a) In the event that any holder of Series B Preferred Shares becomes a Defaulting Investor, then as of the applicable Second Closing (as defined in the Series B Share Purchase Agreement (i) each one share of the Series B-1 Preferred Shares held by such holder, (ii) each one share of Series B-2 Preferred Shares held by such holder and (iii) each one Ordinary Share held by such holder pursuant to the conversion of its Series B-1 Preferred Shares or Series B-2 Preferred Shares shall automatically, and without any further action on the part of such holder or any other person or entity, be converted into one-fifth of one (0.2) Ordinary Share, effective immediately after the Second Closing and whether or not the certificates representing such shares are surrendered to the Company or its transfer agent. Such conversion is referred to as a "***Special Mandatory Conversion***".

(b) Upon any Special Mandatory Conversion specified in Regulation 8.1.12(a) above, the Company shall not be obligated to issue certificates evidencing the Ordinary Shares issuable upon such conversion unless the certificate or certificates evidencing the shares of Series B Preferred Shares automatically converted in such Special Mandatory Conversion are either delivered by the holder to the Company or its transfer agent, or the holder notifies the Company or its transfer agent that such certificate or certificates have been lost, stolen or destroyed and executes an agreement satisfactory to the Company to indemnify the Company from any loss incurred by it in connection with such certificate or certificates. Thereupon, the Company shall issue and deliver to such holder promptly and in its name as shown on such surrendered certificate or certificates, a certificate or certificates for the number of Ordinary Shares into which such holder's shares of Series B Preferred Shares and/or Ordinary Shares were converted in such Special Mandatory Conversion.

8.1.13. **Fractional Shares.** No fractional Ordinary Shares shall be issued upon conversion of Series Preferred Shares. All Ordinary Shares (including fractions thereof) issuable upon conversion of more than one share of Series Preferred Shares by a holder thereof shall be aggregated for purposes of determining whether the conversion would result in the issuance of any fractional share. If after the aforementioned aggregation the conversion would result in the issuance of any fractional share, the Company shall, in lieu of issuing any fractional share, pay cash equal to the product of such fraction multiplied by the fair market value of one share of Ordinary Shares (as determined in good faith by the Board) on the date of conversion.

8.1.14. **Notices.** Any notice required by the provisions of this Regulation 8 shall be in writing and shall be deemed effectively given: (i) upon personal delivery to the party to be notified, (ii) when sent by electronic transmission in compliance with the provisions of the Act if sent during normal business hours of the recipient; if not, then on the next business day, (iii) five days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (iv) one day after deposit with a recognized overnight courier, specifying next day delivery, with verification of receipt. All notices shall be addressed to each holder of record at the address of such holder appearing on the books of the Company.

8.1.15. **Payment of Taxes.** The Company will pay all taxes (other than taxes based upon income) and other governmental charges that may be imposed with respect to the issue or delivery of Ordinary Shares upon conversion of shares of Series Preferred Shares, excluding any tax or other charge imposed in connection with any transfer involved in the issue and delivery of Ordinary Shares in a name other than that in which the shares of Series Preferred Shares so converted were registered.

9. **No Reissuance of Series Preferred Shares.**

9.1. Any shares of Series Preferred Shares redeemed, purchased, converted or exchanged by the Company shall be cancelled and shall not be reissued or transferred.

10. **Transfer of Shares**

10.1. Except as otherwise provided herein, no holder of any of the shares of the Company may sell, transfer, assign, pledge, or otherwise dispose of or encumber any of the shares of the Company or any right or interest therein, whether voluntarily or by operation of law, or by gift or otherwise (each, a "***Transfer***") without the prior written consent of the Board. The Board may withhold such consent for any legitimate corporate purpose, as determined by the Board but is required to consent to Transfers which are permitted in accordance with the terms and conditions set out in the Shareholders Agreements. Examples of the basis for the Board to withhold its consent include, without limitation, (i) if such Transfer to individuals, companies or any other form of entity identified by the Board as a potential competitor or considered by the Board to be unfriendly; or (ii) if such Transfer increases the risk of the Company having a class of security held of record by 2,000 or more persons, or 500 or more persons who are not accredited investors (as such term is defined by the SEC), as described in Section 12(g) of the Securities Exchange Act of 1934 (the "**1934 Act**") and any related regulations, or otherwise requiring the Company to register any class of securities under the 1934 Act; or (iii) if such Transfer would result in the loss of any federal or state securities law exemption relied upon by the Company in connection with the initial issuance of such shares or the

issuance of any other securities; or (iv) if such Transfer is facilitated in any manner by any public posting, message board, trading portal, internet site, or similar method of communication, including without limitation any trading portal or internet site intended to facilitate secondary transfers of securities; or (v) if such Transfer is to be effected in a brokered transaction; or (vi) if such Transfer represents a Transfer of less than all of the shares then held by the shareholder and its Affiliates or is to be made to more than a single transferee. Notwithstanding the forgoing, the Transfers detailed in Regulation 11.1.6 below shall not require the prior written consent of the Board.

10.1.1. If a shareholder desires to Transfer any shares, then subject to the terms of the Shareholders Agreements, the shareholder shall first give written notice thereof to the Company. The notice shall name the proposed transferee and state the number of shares to be transferred, the proposed consideration, and all other terms and conditions of the proposed transfer. Any shares proposed to be transferred as part of a Transfer to which the Board has consented pursuant to 10.1 of this Regulation 10 will first be subject to the Company's right of first refusal provided for in Regulation 11 of this Constitution (subject to any exceptions set out in the Shareholders Agreements).

10.1.2. Any Transfer, or purported Transfer, of shares not made in strict compliance with this Regulation or the terms of the Shareholders Agreements shall be null and void, shall not be recorded on the books of the Company and shall not be recognized by the Company.

10.1.3. The foregoing restriction on Transfer shall terminate upon the date securities of the Company are first offered to the public pursuant to a registration statement filed with, and declared effective by, the SEC under the Securities Act of 1933, as amended (the "***1933 Act***").

10.1.4. The certificates representing shares of the Company shall bear on their face the following legend so long as the foregoing Transfer restrictions are in effect: "THE SHARES REPRESENTED BY THIS CERTIFICATE ARE SUBJECT TO A TRANSFER RESTRICTION, AS PROVIDED IN THE CONSTITUTION OF THE COMPANY."

10.1.5. The Board shall not withhold its consent under this Regulation 10.1 to any Transfer by any Investor where such Transfer is made in accordance with the provisions of any right of first refusal and co-sale, investor rights and/or voting agreement relating to the Company dated on or about the date of adoption of this Constitution.

10.1.6. The Board shall not register a Transfer unless the relevant transferee(s) has executed a deed of adherence to the Shareholders Agreements in a form approved of by the Board.

10.2. The instrument of transfer of any share shall be executed by or on behalf of the transferor, save that if the share concerned (or one or more of the shares concerned) is not fully paid, the instrument shall be executed by or on behalf of the transferor and the transferee.

10.3. Without prejudice to the powers of the directors under Section 95(2) of the Act, the directors may, in their absolute discretion, and without giving any reason for doing so, decline to register any transfer of any share, whether or not it is a fully paid share. The restriction on the power to decline to register a transfer of shares contained in Section 95(1)(b) of the Act shall not apply. Notwithstanding the foregoing, the Board shall not

decline to register any transfer of any share by any Investor where such transfer is made in accordance with the provisions of any right of first refusal and co-sale, investor rights and/or voting agreement relating to the Company dated on or about the Date of Adoption.

10.4. In the event that the Board and the Requisite Super Majority approve a Liquidation Event (each, a "***Sale of the Company***"), then each Shareholder and the Company hereby agree:

10.4.1. if such transaction requires Shareholder approval, with respect to all Shares that such Shareholder owns or over which such Shareholder otherwise exercises voting power, to vote (in person, by proxy or by action by written consent, as applicable) all Shares in favor of, and adopt, such Sale of the Company (together with any related amendment to the Constitution required in order to implement such Sale of the Company) and to vote in opposition to any and all other proposals that could delay or impair the ability of the Company to consummate such Sale of the Company;

10.4.2. if such transaction is in the form of a sale of shares (a "Share Sale"), to sell the same proportion of share capital of the Company beneficially held by such Shareholder as is being sold by the Requisite Super Majority to the person or entity to whom the Requisite Super Majority propose to sell their Shares, on the same terms and conditions as the Requisite Super Majority (except that the proceeds shall be distributed in accordance with Regulation 37);

10.4.3. to execute and deliver all related documentation and take such other action in support of the Sale of the Company as shall reasonably be requested by the Company or the Requisite Super Majority in order to carry out the terms and provision of this Regulation 10.4, including, without limitation, executing and delivering instruments of conveyance and transfer, and any purchase agreement, merger agreement, indemnity agreement, escrow agreement, consent, waiver, governmental filing, share certificates duly endorsed for transfer (free and clear of impermissible liens, claims and encumbrances), and any similar or related documents, provided, however, that the representations and warranties required from Shareholders in such documentation shall be limited to ownership, title and ability to transfer such shares in the Sale of Company Transaction free and clear of any liens, no Shareholder shall be liable under such documentation for the breach of a representation, warrant, covenant or agreement of any other Shareholder (except to the extent paid out of an established escrow on a pro rata basis), and any indemnification obligation or potential liability of such Shareholder shall in no event be in excess of the total consideration to be received by such Shareholder in the Sale of the Company;

10.4.4. not to deposit, and to cause their Affiliates not to deposit, except as provided in the Constitution, any Shares owned by such party or Affiliate in a voting trust or subject any Shares to any arrangement or agreement with respect to the voting of such Shares, unless specifically requested to do so by the acquiror in connection with the Sale of the Company;

10.4.5. to refrain from exercising any dissenters' rights or rights of appraisal under applicable law at any time with respect to such Sale of the Company;

10.4.6. if the consideration to be paid in exchange for the Shares pursuant to this Regulation 10.4 includes any securities and due receipt thereof by any Shareholder would require under applicable law (x) the registration or qualification of such securities or of any person as a broker or dealer or agent with respect to such securities; or (y) the provision to any Shareholder of any

information other than such information as a prudent issuer would generally furnish in an offering made solely to "accredited investors" as defined in Regulation D promulgated under the 1933 Act, the Company may cause to be paid to any such Shareholder in lieu thereof, against surrender of the Shares which would have otherwise been sold by such Shareholder, an amount in cash equal to the fair value (as determined in good faith by the Company) of the securities which such Shareholder would otherwise receive as of the date of the issuance of such securities in exchange for the Shares; and

10.4.7. in the event that the Requisite Super Majority, in connection with such Sale of the Company, appoint a Shareholder representative (the "***Shareholder Representative***") with respect to matters affecting the Shareholders under the applicable definitive transaction agreements following consummation of such Sale of the Company, (x) to consent to (i) the appointment of such Shareholder Representative, (ii) the establishment of any applicable escrow, expense or similar fund in connection with any indemnification or similar obligations, and (iii) the payment of such Shareholder's pro rata portion (from the applicable escrow or expense fund or otherwise) of any and all reasonable fees and expenses to such Shareholder Representative in connection with such Shareholder Representative's services and duties in connection with such Sale of the Company and its related service as the representative of the Shareholders, and (y) not to assert any claim or commence any suit against the Shareholder Representative or any other Shareholder with respect to any action or inaction taken or failed to be taken by the Shareholder Representative in connection with its service as the Shareholder Representative, absent fraud or willful misconduct.

10.4.8. Each existing shareholder has granted (and any future shareholder undertakes to each other shareholder to grant) an irrevocable proxy and power of attorney in connection with a Sale of the Company as set out in the voting agreement which forms part of the Shareholders Agreements.

11. **Right of First Refusal**

11.1. No shareholder shall Transfer any of the shares of the Company, except by a Transfer which meets the requirements set forth in this Regulation 11 or is permitted by the Shareholders Agreement, in addition to any other restrictions or requirements set forth under applicable law or this Constitution:

11.1.1. If the shareholder desires to Transfer any of his or her shares, then the shareholder shall first give written notice thereof to the Company. The notice shall name the proposed transferee and state the number of shares to be transferred, the proposed consideration, and all other terms and conditions of the proposed transfer.

11.1.2. For 30 days following receipt of such notice, the Company shall have the option to acquire up to all the shares specified in the notice at the price and upon the terms set forth in such notice (subject to the provisions of the Act); *provided, however,* that, with the consent of the proposed transferor, the Company shall have the option to acquire a lesser portion of the shares specified in said notice at the price and upon the terms set forth therein. In the event of a gift, property settlement or other Transfer in which the proposed transferee is not paying the full price for the shares, and that is not otherwise exempted from the provisions of this Regulation 11, the price shall be deemed to be the fair market value of the shares at such time as determined in good faith by the Board. In the event the Company elects to acquire all of the shares or, with consent of the shareholder, a lesser portion of the shares, it shall give written notice to the

transferring shareholder of its election and settlement for said shares shall be made as provided below in 11.1.4 of this Regulation 11.

11.1.3. The Company may assign its rights hereunder to any other Group Company.

11.1.4. In the event the Company and/or its assignee(s) elect to acquire any of the shares of the transferring shareholder as specified in said transferring shareholder's notice, the Secretary of the Company shall so notify the transferring shareholder and settlement thereof shall be made in cash within 30 days after the Secretary of the Company receives said transferring shareholder's notice; provided that if the terms of payment set forth in said transferring shareholder's notice were other than cash against delivery, the Company and/or its assignee(s) shall pay for said shares on the same terms and conditions set forth in said transferring shareholder's notice.

11.1.5. In the event the Company and/or its assignees(s) do not elect to acquire all of the shares specified in the transferring shareholder's notice, said transferring shareholder may, subject to the Company's approval and all other restrictions on Transfer provided for in Regulation 10 of this Constitution, within the 60-day period following the expiration or waiver of the option rights granted to the Company and/or its assignees(s) herein, Transfer the shares specified in said transferring shareholder's notice which were not acquired by the Company and/or its assignees(s) as specified in said transferring shareholder's notice. All shares so sold by said transferring shareholder shall continue to be subject to the provisions of this Constitution in the same manner as before said Transfer.

11.1.6. Anything to the contrary contained herein notwithstanding, the following transactions shall be exempt from the right of first refusal in 11.1.2 of this Regulation 11:

(1) A shareholder's Transfer of any or all shares held either during such shareholder's lifetime or on death by will or intestacy to such shareholder's immediate family or to any custodian or trustee for the account of such shareholder or such shareholder's immediate family or to any limited partnership of which the shareholder, members of such shareholder's immediate family or any trust for the account of such shareholder or such shareholder's immediate family will be the general or limited partner(s) of such partnership. "**Immediate family**" as used herein shall mean spouse, lineal descendant, father, mother, brother, or sister of the shareholder making such Transfer;

(2) A shareholder's Transfer of any or all of its shares pursuant to and in accordance with the terms of any sale, scheme of arrangement, merger, consolidation, reclassification of shares or capital reorganization of the shareholder, or pursuant to a sale of all or substantially all of the stock or assets of a shareholder;

(3) A shareholder's Transfer of Series Preferred Shares of the Company (or any Ordinary Shares issued upon conversion thereof);

(4) A shareholder's Transfer of any or all of its shares to any or all of its shareholders;

(5) A Transfer by a shareholder which is a limited or general partnership to any or all of its partners or former partners in accordance with partnership interests; or

(6) A Transfer by a shareholder which is a corporation to any parent corporation or wholly-owned subsidiary of such corporation, or any direct or indirect wholly-owned subsidiary of the ultimate parent entity of such corporation.

In any such case, the transferee, assignee, or other recipient shall receive and hold such shares subject to the provisions of this Regulation 11 and any other restrictions set forth in this Constitution, and there shall be no further Transfer of such shares except in accord with this Regulation 14 and the other provisions of this Constitution.

11.1.7. The provisions of this Constitution may be waived with respect to any Transfer either by the Company, upon duly authorized action of its Board, or by the shareholders, upon the express written consent of the owners of a majority of the voting power of the Company (excluding the votes represented by those shares to be transferred by the transferring shareholder).

11.1.8. Any Transfer, or purported Transfer, of securities of the Company shall be null and void unless the terms, conditions, and provisions of this Regulation 11 are strictly observed and followed.

11.1.9. The foregoing right of first refusal shall terminate upon the date securities of the Company are first offered to the public pursuant to a registration statement filed with, and declared effective by, the SEC under the 1933 Act, as amended, or on any other market exchange approved by the Board.

11.1.10. The certificates representing Ordinary Shares of the Company that are subject to the right of first refusal in 11.1.1 of this Regulation 11 shall bear on their face the following legend so long as the foregoing right of first refusal remains in effect: “THE SHARES REPRESENTED BY THIS CERTIFICATE ARE SUBJECT TO A RIGHT OF FIRST REFUSAL OPTION IN FAVOR OF THE COMPANY AND/OR ITS ASSIGNEE(S), AS PROVIDED IN THE CONSTITUTION OF THE COMPANY.”

11.1.11. To the extent this Regulation 11 conflicts with any written agreements between the Company and the shareholder attempting to Transfer shares, such agreement shall take precedence.

12. **Transmission of Shares by Operation of Law in Consequence of a Merger:**

12.1. In any case in which any share or shares in the Company (Relevant Shares) which are held by another company or body corporate, wherever incorporated (the Corporate Member) is or are transmitted by operation of law in consequence of a merger involving the Corporate Member and one or more other companies (which may include the Company) or bodies corporate, wherever incorporated, and which is put into effect in accordance with the provisions in that regard contained in the Act, in the European Communities (Cross-Border Mergers) Regulations 2008 (S.I. No. 157 of 2008) (as amended), or in any other applicable law or other enactment (a merger) and if, in any such case, the provisions of Section 480(6) of the Act are not applicable for any reason, a transfer of the Relevant Shares may be validly effected in accordance with the following provisions of this Regulation.

12.2. In any case as is mentioned in the foregoing paragraph 12.1 of this Regulation, any person who is or who becomes entitled to any Relevant Shares in consequence of any such merger (a Relevant Person) may, subject always to paragraph 12.3 of this Regulation, upon such evidence being produced as may from time to time be required by the directors of the Company (including without limitation any information and documentation relating to the merger and the title and other rights of the Relevant Person

to the Relevant Shares arising as a result thereof) elect either to be registered himself in the register as holder of the Relevant Shares, or, to the extent permitted by law, to have some person nominated by him (being a person who consents to be so registered) registered in the register as the transferee thereof.

12.3. The directors of the Company shall, in either of those cases, have the same rights under the Act or this Constitution to decline or suspend registration as they would have had in the case of a transfer of the Relevant Shares by the Corporate Member before the merger was put into effect as aforesaid.

12.4. If the Relevant Person elects to be so registered himself, the Relevant Person shall furnish to the Company a notice in writing signed by him stating that he so elects, and if the Relevant Person elects, to the extent permitted by law, to have another person registered instead, the Relevant Person shall testify his or her election by executing in favour of that other person a transfer of the Relevant Shares.

12.5. All the limitations, restrictions and provisions contained in the Act or in this Constitution relating to the right to transfer and the registration of a transfer of a share shall be applicable to a notice or transfer referred to in paragraph 12.4 of this Regulation as if the merger had not occurred and the notice or transfer were a transfer signed by the Corporate Member.

12.6. Subject to paragraph 12.7 of this Regulation, the Relevant Person (or any other person nominated by him, to the extent permitted by law, in accordance with the foregoing provisions of this Regulation) shall, on and from the effective date of the merger, be entitled to the same dividends, bonus and other monies payable in respect of the Relevant Shares and other advantages to which he would be entitled if he was the registered holder of the Relevant Shares but shall not, before being registered in the register as a member in respect of the Relevant Shares, be entitled in respect of them to exercise any rights conferred by membership in relation to meetings of the Company.

12.7. The directors of the Company may at any time serve a notice on any Relevant Person requiring the Relevant Person to make the election, to the extent permitted by law, provided for by paragraph 12.2 of this Regulation and, if the person does not make that election (and proceed to do, consequent on that election, whichever of the things mentioned in paragraph 12.4 of this Regulation is appropriate) within 90 days after the service of the notice, the directors may thereupon withhold payment of all dividends, bonuses or other monies payable in respect of the Relevant Shares until the requirements of the notice have been complied with.

12.8. The Company may charge a fee not exceeding €10 on the registration of any person entitled to a share in consequence of a merger in accordance with the foregoing provisions of this Regulation.

12.9. The provisions of this Regulation shall be subject to any order made by a court having lawful jurisdiction in respect of a merger.

13. **Acquisition of Own Shares:** Subject to (and without prejudice to) the provisions of the Act, the Company may acquire its own shares by purchase, or in the case of redeemable shares, by redemption or purchase, on such terms (including as to the consideration for, and the timing of, any such purchase or redemption) and in such a manner as shall be determined by the directors in their absolute discretion.

14. **Directors:**

14.1. **Director Matters**

14.1.1. **Number of Directors:** The number of directors from time to time shall be at least two and not more than ten (unless approved of by a Requisite Super Majority).

14.1.2. Quorum: The quorum necessary for the transaction of the business of the directors shall be three in person or by alternate (provided always that the majority of the directors constituting the quorum shall be Series Preferred Directors). If within half an hour from the time appointed for the meeting a quorum (with the majority of the directors constituting the quorum being Series Preferred Directors) is not present, the meeting, shall be adjourned to the same day in the next week at the same time and place, or to such other day and at such other time and place as the Board may determine, and if at the adjourned meeting a quorum (provided always that the majority of the directors constituting the quorum shall be Series Preferred Directors) is not present within half an hour from the time appointed for the meeting, the directors present shall be a quorum provided only those matters as specifically sent out in the agenda for the initial meeting are put before the adjourned meeting.

14.1.3. Board Meetings: The directors may meet together for the dispatch of business, adjourn and otherwise regulate their meetings as they think fit. Questions arising at any such meeting shall be decided by a majority of votes of those directors present and counted towards the quorum at that meeting and where there is an equality of votes, the chairperson shall not have a second or casting vote. A director may, and the secretary on the requisition of a director shall, at any time summon a meeting of the directors. Any director (including an alternate) or any member of a committee of directors may participate in a meeting of the directors or a committee of directors of which he is a member by means of a conference telephone or similar communicating equipment whereby all persons participating in the meeting can hear each other, and participation in a meeting in this manner will be deemed to constitute presence in person (or, as the case may be, by alternate) at such meeting and, for the purposes of determining whether the quorum for the transaction of business exists, any directors or committee member in telephonic communication with a meeting of directors or of a committee as the case may be will be counted in the quorum. Such meeting shall be deemed to be held at the place where the chairman of the meeting is present or if otherwise agreed in the place where the person who originated the telephonic communication is present and the word "Meeting" where used in this Constitution in the context of the meeting of the directors or any committee thereof shall be construed accordingly.

14.1.4. **General:** The business of the Company shall be managed by the directors, who may pay all expenses incurred in promoting and registering the Company and may exercise all such powers of the Company as are not, by the Act or by these Regulations, required to be exercised by the Company in general meeting, subject, nevertheless, to any of these Regulations, to the provisions of the Act and to such directions, being not inconsistent with the aforesaid regulations or provisions, as may be given by the Company in general meeting; but no direction given by the Company in general meeting shall invalidate any prior act of the directors which would have been valid if that direction had not been given. The Board may from time to time and at any time by power of attorney appoint any company, firm or person or body of persons, whether nominated directly or indirectly by the directors, to be the attorney or attorneys of the Company for such purposes and with such powers, authorities and discretions (not exceeding those vested in or exercisable by the directors under these Regulations) and for such period and subject to such conditions as they may think fit, and any such power of attorney may contain such provisions for the protection of persons dealing with any such attorney as the directors may think fit, and may also

authorise any such attorney to delegate all or any of the powers, authorities and discretions vested in him.

14.1.5. **Minutes:** The directors shall cause minutes to be made in books provided for the purpose -

(a) of all appointment of officers made by the directors;

(b) of the names of the directors present at each meeting of the directors and of any committee of the directors; and

(c) of all resolutions and proceedings at all meetings of the Company and of the directors and of committees of directors.

14.2. **Election of Board of Directors:**

14.2.1. For so long as any shares of Series A Preferred Shares remain outstanding, the holders of Series A Preferred Shares, voting as a separate class, shall be entitled to appoint and remove (either at a meeting of the holders of the Series A Preferred Shares or by notice in writing signed by the relevant Investor listed in this Regulation 14.2.1 as having an entitlement to appoint a director) up to four members to the Board and to fill any vacancy caused by the resignation, death or removal of such directors, in each case by notice in writing to the Company secretary and in accordance with the provisions of any voting agreement relating to the Company dated on or about the date of adoption hereof. At the date of adoption the four members of the Board to be appointed by the holders of the Series A Preferred Shares shall be:

(1) one individual designated by Frazier Healthcare VII, L.P. and Frazier Healthcare VII-A, L.P. (collectively, "Frazier") so long as Frazier does not become a Defaulting Investor;

(2) one individual designated by Canaan Partners so long as it does not become a Defaulting Investor;

(3) one individual designated by New Leaf Venture Partners so long as it does not become a Defaulting Investor; and

(4) one individual designated by Sofinnova Ventures so long as it does not become a Defaulting Investor.

14.2.2. For so long as any shares of Series B Preferred Shares remain outstanding, the holders of Series B Preferred Shares, voting as a separate class, shall be entitled to appoint and remove (either at a meeting of the holders of the Series B Preferred Shares or by notice in writing signed by the relevant Investor listed in this Regulation 14.2.2 as having an entitlement to appoint a director) up to three members to the Board and to fill any vacancy caused by the resignation, death or removal of such directors, in each case by notice in writing to the Company secretary and in accordance with the provisions of any voting agreement relating to the Company dated on or about the date of adoption hereof. At the date of adoption the one member of the Board to be appointed by the holders of the Series B Preferred Shares shall be:

(1) one individual designated by Arix Biosciences Holdings Ltd. ("**Arix**") so long as Arix does not become a Defaulting Investor;

(2) one individual designated by Advent Life Sciences LLP and Advent Life Sciences Fund II LP (collectively, "**Advent**") so long as Advent does not become a Defaulting Investor; and

(3) one individual designated by Pivotal bioVenture Partners Fund I, L.P. ("**Pivotal**") so long as Pivotal does not become a Defaulting Investor.

14.2.3. The holders of Ordinary Shares, voting as a separate class, shall be entitled to appoint one member to the Board (being the person then serving as chief executive officer) and to remove from office such director (where he/she ceases to be the chief executive officer), in each case by notice in writing to the company secretary and in accordance with the provisions of any voting agreement relating to the Company dated on or about the date of adoption.

14.2.4. The holders of Ordinary Shares and Series Preferred Shares, voting together as a single class on an as-if-converted basis, shall be entitled to appoint and remove (by notice in writing or by vote at a general meeting) all remaining members to the Board and to fill any vacancy caused by the resignation, death or removal of such directors, in each case by notice in writing to the company secretary and in accordance with the provisions of any voting agreement relating to the Company dated on or about the date of adoption hereof.

14.2.5. Any vacancy, including newly created directorships resulting from any increase in the authorized number of directors or amendment of this Constitution, and vacancies created by removal or resignation of a director, may be filled by a majority of the directors then in office, though less than a quorum, or by a sole remaining director, and the directors so chosen shall hold office until the next annual election and until their successors are duly elected and shall qualify, unless sooner displaced; provided, however, that where such vacancy occurs among the directors elected by the holders of a class or series of shares, the holders of shares of such class or series may override the Board's action to fill such vacancy by (i) voting for their own designee to fill such vacancy at a meeting of the Company's shareholders or (ii) written consent, if the consenting shareholders hold a sufficient number of shares to elect their designee at a meeting of the shareholders in which all members of such class or series are present and voted. Any director may be removed during his or her term of office without cause, by, and only by, the affirmative vote of the holders of the shares of the class or series of shares entitled to elect such director or directors, given either at a special meeting of such shareholders duly called for that purpose or pursuant to a written consent of shareholders, and any vacancy thereby created may be filled by the holders of that class or series of shares represented at the meeting or pursuant to written consent. At any meeting held for the purpose of electing a director, the presence in person or by proxy of the holders of a majority of the outstanding shares of the class or series entitled to elect such director shall constitute a quorum for the purpose of electing such director.

15. **Committees of Directors:** The directors may delegate any of their powers to committees consisting of such member or members of the board as they think fit provided however that each Committee shall include at least a majority of Series Preferred Directors; any committee so formed shall, in the exercise of the powers so delegated, conform to any regulations that may be imposed on it by the directors. A committee may elect a chairman of its meetings; if no such chairman is elected, or if at any meeting the chairman is not present within 5 minutes after the time appointed for holding the same, the members present may choose one of their number to be chairman of the meeting. A committee may meet and adjourn as it thinks proper. Questions arising at any meeting shall be determined by a majority of votes of the members present, and where there is an equality of votes, the chairman shall not have a second or casting vote. All acts

done by any meeting of the directors or of a committee of directors or by any person acting as a directors shall, notwithstanding that it be afterwards discovered that there was some defect in the appointment of any such directors or person acting as aforesaid, or that they or any of them were disqualified, be as valid as if every such person had been duly appointed and was qualified to be a director. The meetings and proceedings of any committee formed by the directors will be governed by the provisions set out in the Act regulating the meetings and proceedings of directors so far as the same are applicable and are not superseded by any regulations imposed on such committee by the directors from time to time. Each Series Preferred Director shall be entitled (at his discretion) to be appointed to each committee established by the Board.

16. **Vacation of Office of Director:**

16.1. The office of a director shall, in addition to the circumstances in which it shall be vacated described in Section 136 (share *qualification, if applicable*) and Section 148(1) (*bankruptcy and disqualification*), also be vacated automatically if the director dies in office, or if the director:

16.1.1. becomes subject to a declaration of restriction made pursuant to Chapter 3 of Part 14 of the Act;

16.1.2. is sentenced to a term of imprisonment following conviction of any indictable offence, unless the term of imprisonment is suspended, such that he is not imprisoned in respect of the offence;

16.1.3. is no longer reasonably regarded by his co-directors as possessing an adequate decision-making capacity for reasons of health, and his co-directors have accordingly resolved that his office be vacated on this ground, or he becomes the subject of an order made in Ireland or elsewhere by a court claiming jurisdiction in that regard for his detention or for the appointment of a guardian or other person to exercise powers with respect to his property or affairs, on the ground, in any such case, of mental disorder or incapacity;

16.1.4. resigns his office by notice in writing to the Company; or

16.1.5. makes any arrangement or composition in Ireland or elsewhere with his creditors generally, and his co-directors resolve, for that reason, that his office be vacated.

16.2. The provisions of paragraphs 16.1.1 to 16.1.5 of this Regulation shall apply to the exclusion of the provisions of Section 148(2) of the Act.

17. **Alternate Directors:**

17.1. Any director (the appointer) may at any time and from time to time appoint by notice in writing to the Company any person to be his alternate.

17.2. A person may act as an alternate for more than one director and while he is so acting will be entitled to a separate vote for each director he is representing and, if he is himself a director, his vote or votes as an alternate will be in addition to his own vote.

17.3. An alternate will be counted for the purpose of reckoning whether a quorum is present at any meeting attended by him at which he is entitled to vote, but where he is himself a director or is the alternate of more than one director he will only be counted once for such purpose.

17.4. An alternate will be entitled, subject to his giving to the Company an address to receive notice of all meetings of the directors and of all meetings of committees of which his appointer is a member, to receive notice of and attend and vote at any meeting of the

directors (or of a committee of which his appointer is a member) at which the appointer is not personally present. An alternate shall not be entitled to be remunerated or paid fees otherwise than out of the remuneration or fees as the case may be paid to the appointer.

17.5. The alternate will be entitled, in the absence of the appointer, to exercise all the powers, rights, duties and authorities of the appointer as a director (other than the right to appoint an alternate hereunder).

17.6. An alternate's appointment will automatically come to an end if for any reason the appointer ceases to be a director, but if a director retires but is re-appointed or deemed to have been re-appointed at the meeting at which he retires, any appointment of an alternate made by him which was in force immediately prior to his retirement will continue after his re-appointment. Section 165(5) and (6) of the Act in relation to revocation of appointment shall apply.

18. **Managing and Executive Directors:**

18.1. Subject to the other provisions of this Constitution, the directors may from time to time appoint one or more of themselves to be managing director or chief executive officer or any other category of executive director (by whatever name called) for such period, and on such terms as to remuneration or otherwise, as they think fit and, subject to the terms of any agreement entered into in any particular case, may revoke such appointment. The directors may entrust to and confer upon any director so appointed any of the powers exercisable by them upon such terms and conditions and with such restrictions (if any) as they may think fit, and either concurrently with or to the exclusion of their own powers, and may from time to time revoke, withdraw, alter or vary all or any conferral of such powers. Section 159(2) of the Act shall not apply in relation to any such appointment.

19. **Directors' Contracts:**

19.1. Notwithstanding the provisions of Section 162 of the Act, no contract will be entered into by the Company for the employment of, or the provision of services by, a director or a director of a holding company of the Company containing a term to which Section 249 of the Act applies, without obtaining the approval provided for in that Section.

20. **Directors' Right to Attend Meetings:**

20.1. A director who is not a member of the Company will nevertheless be entitled to receive notice of, attend and speak at any general meeting or separate meeting of the holders of any class of share.

21. **Voting by Directors:**

21.1. A director may vote in respect of any contract, appointment or arrangement in which he is interested, and he shall be counted in the quorum present at any meeting at which such matters are considered. Section 163 of the Act shall not apply.

22. **Remuneration of Directors:**

22.1. The remuneration which shall include benefits in kind, and any fees, to be paid to directors of the Company shall be at such rate and basis as the directors shall determine from time to time. The directors shall also be entitled to be paid their travelling, hotel and other expenses properly incurred by them in attending and returning from meetings of the directors or any committee of the directors or general meetings of the Company or otherwise in connection with the business of the Company, or to receive a fixed allowance in respect thereof as may be determined by the directors from time to time, or a combination partly of one such method and partly of the other. The amount, rate or

basis of the fees, remuneration or expenses paid or to be paid to the directors shall not require the approval of or ratification by the Company in general meeting.

22.2. The board may approve additional remuneration to any director undertaking any special work or services for, or undertaking any special task on behalf of the Company including participating as a member of a committee, in addition to his ordinary work as a director. Any remuneration or fees paid by a director who is also a legal adviser to the Company or otherwise serves the Company in a professional capacity shall be in addition to any remuneration or fees paid to him as a director of the Company.

23. **Resolutions in Writing:**

23.1. Notwithstanding the provisions of Section 161(1) of the Act, a resolution in writing signed by each director or by his alternate will be as valid as if it had been passed at a meeting of the directors duly convened and held.

23.2. A resolution in writing signed by each member of a committee (or, in the case of a director, his alternate) will be as valid as if it had been passed at a meeting of that committee duly convened and held.

23.3. Any such resolution as is referred to in this Regulation may consist of one document or two or more documents in like form to the same effect, each signed by one or more of the signatories, and for all purposes shall take effect from the time that it is signed by the last such signatory.

24. **Certain matters not to amount to conflicts of interest, etc.:**

24.1. A director who has been validly appointed or nominated for appointment by a particular member or members may (i) be a director or other officer of, employed by or otherwise interested (including by the holding of shares) in, any such member or members, or of any body corporate owned or controlled by any such member or members, and (ii) have regard to the interests of that member or members, and shall not be deemed to have a conflict of interest or to be in breach of his duty under Section 228(1)(f) of the Act in any such circumstances.

24.2. A director who declares the nature of his interest in a contract (as the expression contract is to be interpreted by Section 231 of the Act) or proposed contract with the Company in accordance with the requirements of the Act in that regard shall not be deemed to be in breach of his duty under Section 228(1)(f) of the Act, but this is without prejudice to the powers of the directors to take any action which they may consider appropriate in their discretion in relation to any matters so disclosed.

25. **Directors' and Officers' Interests:** A director may be counted in determining the presence of a quorum at a meeting of the Board which authorises or approves a contract, transaction or arrangement in which he or she is interested and he or she shall be at liberty to vote in respect of any contract, transaction or arrangement in which he or she is interested, provided that the nature of the interest of any director in any such contract or transaction shall be disclosed by him or her in accordance with Section 231 of the Act, at or prior to its consideration and any vote thereon. Regulation 25 shall apply to the exclusion of the provisions of Section 1113 of the Act.

26. **Use of Company property:**

26.1. Unless the members of the Company in general meeting shall otherwise determine, and subject always to the other Regulations of this Constitution, any director may use, for his own benefit, any of the Company's property where the other directors or the members of the Company have given their consent (whether express or implied) to that use.

27. **Proxies:**

27.1. The instrument appointing a proxy shall be in the form prescribed by the Act, or as near to it as circumstances permit. The instrument of proxy and the power of attorney or other authority, if any, under which it is signed, or a notarially certified copy of that power or authority, shall be deposited at the registered office of the Company or at such other place within Ireland as is specified for that purpose in the notice convening the meeting of the Company, and shall be so deposited not later than before the commencement of the meeting or adjourned meeting at which the person named in the instrument proposes to vote or, in the case of a poll, before the commencement of the taking of the poll.

27.2. The directors or the secretary may from time to time permit appointments of a proxy to be made by means of an electronic or internet communication or facility or by facsimile transmission, and may permit supplements, amendments or revocations of any such appointments to be made by similar means. Any such appointments of proxy and any such supplements, amendments or revocations thereof may be made subject to such terms and conditions as the directors or secretary may determine from time to time in their or his discretion, and any such appointments, supplements, amendments or revocations of proxy will be deemed deposited at the place specified for such purpose, once received by the Company. The directors may treat any such communication, facility or transmission which purports to be or is expressed to be sent on behalf of a member as sufficient evidence of the authority of the person sending it to send it on behalf of that member.

27.3. Any body corporate which is a member of the Company may, by resolution of its directors or other governing body, authorise such person as it thinks fit to act as its representative at any meeting of the Company or of any class of members of the Company, and the person so authorised shall be entitled to exercise the same powers on behalf of the body corporate which he represents as that body corporate could exercise if it were an individual member of the Company.

28. **Business of AGM:** Without prejudice to the powers of the directors to include on the agenda of any annual general meeting of the Company such other matters as they may, in their absolute discretion, think fit, the business of the annual general meeting of the Company shall be required to include only the following matters:

28.1. the consideration of the Company's statutory financial statements and the report of the directors and, unless the Company is entitled to and has availed itself of the audit exemption under Section 360 or Section 365 of the Act, the report of the statutory auditors on those statements and that report;

28.2. the review by the members of the Company's affairs; and

28.3. save where the Company is entitled to and has availed itself of the exemption referred to in paragraph 28.1 of this Regulation, the appointment or re-appointment of statutory auditors.

29. **General Meetings outside Ireland:** An annual general meeting or an extraordinary general meeting of the Company may be held inside or outside Ireland provided that, if the Company holds any such meeting outside Ireland then, unless all of the members entitled to attend and vote at such meeting consent in writing to its being held outside Ireland, the Company shall at its own expense make all necessary arrangements to ensure that members can, by technological means, participate in any such meeting without leaving Ireland.

30. **General Meetings**

30.1. **Quorum**: The quorum for general meetings of the Company shall be three members of the Company (including such number of Investors as constitute a Requisite Super Majority) present in person or by proxy unless the Company is a single-member company, in which case one member present in person or by proxy shall be a quorum.

30.2. **Chairperson**: Where there is an equality of votes, whether on a show of hands or on a poll, the chairperson of the meeting at which the show of hands takes place or at which the poll is demanded, shall not have a second or casting vote.

30.3. **EGM**: All general meetings other than annual general meetings shall be called extraordinary general meetings.

30.4. **Proceedings**: No business shall be transacted at a general meeting of the Company unless a quorum of members is present at the time when the meeting proceeds to business. Three members present in person or by proxy shall constitute a quorum (which must include such number of Investors as constitute a Requisite Super Majority). If within 30 minutes from the time appointed for the meeting a quorum is not present, the meeting shall stand adjourned to the same day in the next week at the same time and place as the directors may determine, and if at the adjourned meeting a quorum is not present within 30 minutes from the time appointed for such meeting, the members present shall be a quorum provided that at least any three (3) members are present in person or by proxy provided only those matters specifically sent out in the agenda for the initial meeting are put before the adjourned meeting. The chairman, if any, of the board of directors shall preside as chairman at every general meeting of the Company, or if there is no such chairman, or if he is not present within 15 minutes after the time appointed for the holding of the meeting or is unwilling to act, the directors present shall elect one of their number to be chairman of the meeting. If at any meeting no director is willing to act as chairman or if no director is present within 15 minutes after the time appointed for holding the meeting, the members present shall choose one of their number to be chairman of the meeting. The chairman may, with the consent of any meeting at which a quorum is present, and shall if so directed by the meeting, adjourn the meeting from time to time and from place to place, but no business shall be transacted at any adjourned meeting other than the business left unfinished at the meeting from which the adjournment took place. When a meeting is adjourned for 30 days or more, notice of the adjourned meeting shall be given as in the case of an original meeting. Save as aforesaid it shall not be necessary to give any notice of an adjournment or of the business to be transacted at an adjourned meeting.

30.5. **Votes:** Subject to any rights or restrictions for the time being attached to any class or classes of shares, on a show of hands every member present in person and every proxy shall have one vote, so, however, that no individual shall have more than one vote, and on a poll every member shall have one vote for each share of which he is the holder. Where there are joint holders, the vote of the senior who tenders a vote, whether in person or by proxy, shall be accepted to the exclusion of the votes of the other joint holders; and for this purpose, seniority shall be determined by the order in which the names stand in the register. No member shall be entitled to vote at any general meeting unless all calls or other sums immediately payable by him in respect of shares in the Company have been paid. No objection shall be raised to the qualification of any voter except at the meeting or adjourned meeting at which the vote objected to is given or tendered, and every vote not disallowed at such meeting shall be valid for all purposes. Any such objection made in due time shall be referred to the chairman of the meeting, whose decision shall be final and conclusive. Votes may be given either personally or by proxy. The instrument appointing a proxy shall be in writing under the hand of the appointer or of his attorney duly authorised in writing, or, if the appointer is a body corporate, either under seal or under the hand of an officer or attorney duly authorised. A proxy need not be a member of the Company. The instrument appointing a proxy shall be

deemed to confer authority to demand or join in demanding a poll. A vote in accordance with the terms of an instrument of proxy shall be valid notwithstanding the previous death or insanity of the principal or revocation of the proxy or of the authority under which the proxy was executed or the transfer of the share in respect of which the proxy is given, if not intimation in writing of such death, insanity, revocation or transfer as aforesaid is received by the Company at the office before the commencement of the meeting or adjourned meeting at which the proxy is used. Every person who, by operation of law, transfer or other means shall become entitled to any Share shall be bound by every notice or other document which previous to his or her name and address being entered on the register in respect of that Share, shall have been given to the person in whose name the Share shall have been previously registered.

31. **Right to demand a poll:**

31.1. At any general meeting a poll may be demanded by:

31.2. the chairperson of the meeting;

31.2.1. at least two members present in person or by proxy;

31.2.2. any Investor present in person or by proxy;

31.2.3. any member or members present in person or by proxy and representing not less than 10 per cent of the total voting rights of all the members of the Company having the right to vote at the meeting; or

31.2.4. a member or members holding shares in the Company conferring the right to vote at the meeting being shares on which an aggregate sum has been paid up equal to not less than 10 per cent of the total sum paid up on all the shares conferring that right.

32. **Restriction on voting:** For so long as the Company holds any shares as treasury shares, or any subsidiary of the Company holds shares in the Company, then the Company or the subsidiary (as the case may be) shall not exercise any voting rights in respect of the shares.

33. **Unanimous Written Resolutions and Majority Written Resolutions**

A unanimous written resolution and a majority written resolution may be passed by members subject to and in accordance with Section 193 and Section 194 respectively of the Act.

34. **Directors' and Officers' Indemnity:** Subject to the provisions of the Act, every director, managing director, chief executive officer, secretary and other officer for the time being of the Company shall be indemnified out of the assets of the Company against any liability incurred by him:

34.1. in defending any proceedings, whether civil or criminal, in relation to his acts or omissions while acting in such office, in which judgment is given in his favour or in which he is acquitted; or

34.2. in connection with any proceedings or application referred to in, or under, Sections 233 or 234 of the Act in which relief is granted to him by the court.

35. **Notices:**

35.1. Any notice or document to be served on or given to a member of the Company by the Company or by an officer of the Company whether pursuant to any provision of the Act or this Constitution or otherwise may be served on or given to the member in any of the

ways specified in subsection (3) of Section 218 of the Act (including by electronic means provided that in such a case the conditions specified in subsection (4) of that Section are satisfied), and the notice or document shall be deemed to have been served or given as follows:-

35.1.1. if given personally or delivered to the member, when so given or delivered;

35.1.2. if left at the registered address of the member, when so left at that address;

35.1.3. if the notice is a notice of a general meeting, and it is posted using ordinary pre-paid post to the registered address of the member, on the expiration of 24 hours following posting (as permitted by Section 181(3) of the Act) but in a case where the notice or document is not a notice of a meeting, it shall be deemed to have been given or served 48 hours after the cover containing it was posted, and if so posted on a Friday, 72 hours after it was so posted; and

35.1.4. if served on or delivered to a member by electronic means, both in the case of the service or giving of the notice or document by sending it by electronic mail and by making it available or displaying it on a website, 12 hours after the time it was sent, or made available or displayed.

35.1.5. Where the Company is required or obliged to serve a notice on or give it to a person other than a member of the Company, it shall be in writing and, without prejudice to any method of service provided for in the Act, may be served on or given to that person personally, or by leaving it at or posting it to the last-known postal address of that person, or by sending it to the other person by electronic mail provided that the person has consented to the use of electronic mail to serve or give notices on or to such person and has not, at the time that electronic mail is so used, given written notice to the Company in accordance with the provisions of this Constitution withdrawing that consent. A notice or document given or served in a manner referred to in this paragraph shall be deemed to have been given or served as follows:

35.1.6. if given personally, when so given;

35.1.7. if left at the last-known postal address of the person, when so left at that address;

35.1.8. if posted using ordinary pre-paid post to the last-known postal address of the other person on any day other than a Friday, 48 hours after the cover containing it was posted, and if so posted on a Friday, 72 hours after it was so posted; and

35.1.9. if served on or delivered to the other person by electronic mail, 12 hours after the time it was sent.

35.2. Without prejudice to any provision of the Act or of these Regulations concerning the sending of notices or other documents to the Company, any notice or other document which is required to be served on or given to the Company by a member or by any other person under the Act or this Constitution shall be in writing and in the English language, and may be served on or given to the Company by giving or delivering it personally to the secretary of the Company or by posting it using ordinary pre-paid post to the registered office of the Company marked for the attention of the secretary, and will be deemed to have been served on or given to the Company;

35.2.1. if given or delivered personally, when so given or delivered; and

35.2.2. if posted in the manner described in this paragraph on any day other than a Friday, 48 hours after the cover containing it was posted, and if so posted on a Friday, 72 hours after it was so posted.

36. **Single-member Company:**

36.1. If at any time the Company has only one member, that is to say that all the issued shares of the Company are registered in the name of a sole person (whether a natural person or a body corporate), it will be a single-member company within the meaning of the Act. If and so long as the Company is a single-member company, the sole member may appoint a person to be a director of the Company by serving a notice in writing on the Company which states that the named person is appointed director, and this applies notwithstanding anything in subsection (3) of Section 144 of the Act (save for the requirement of it that any limit for the time being on the number of directors provided for in this Constitution (if any) is to be observed) or in subsection (4) of Section 144.

36.2. Where the Company is a single-member company and the sole member takes any decision which has effect, pursuant to Section 196 of the Act, as if agreed by the Company in general meeting, the member shall provide the Company with a written record of that decision, unless the decision is taken by way of written resolution which the member has already forwarded to the Company, and where the Company is notified by the sole member of a decision taken by way of a written resolution, or of a written record of a decision taken by that sole member, the Company shall record and retain the notification in a book or other suitable means maintained for the purpose.

36.3. Where the Company is a single-member company and the sole member exercises or discharges any power, right or obligation pursuant to Section 196 of the Act, involving or consisting of the passing of a resolution, or the sole member agreeing to a thing, and the provisions of Section 198 shall apply to that resolution or thing, the Company shall notify such exercise or discharge in writing within 15 days of the occurrence thereof to the Registrar of Companies.

36.4. Where the Company is a single-member company and enters into a contract with the sole member which is not in the ordinary course of business and which is not in writing, and the sole member also represents the Company in the transaction (whether as a director or otherwise), the Company shall ensure that the terms of the contract are forthwith set out in a written memorandum or are recorded in the minutes of the next directors' meeting.

37. **Liquidation Rights.**

37.1. Upon any Liquidation Event, before any distribution or payment shall be made to the holders of (i) any Series A Preferred Shares; or (ii) any Ordinary Shares, subject to the right of any of the Series B Preferred Shares that may from time to time come into existence, the holders of the Series B Preferred Shares shall be entitled to be paid out of the assets of the Company legally available for distribution (or the consideration received by the Company or its shareholders in an Acquisition) for each Series B-1 Preferred Share held by them, an amount per share of one Series B-1 Preferred Share equal to the Series B-1 Original Issue Price plus all declared and unpaid dividends on such Series B-1 Preferred Share and for each Series B-2 Preferred Share held by them, an amount per share of one Series B-2 Preferred Share equal to the Series B-2 Original Issue Price plus all declared and unpaid dividends on such Series B-2 Preferred Share. If, upon any such Liquidation Event, the assets of the Company shall be insufficient to make payment in full to all holders of the Series B Preferred Shares of the liquidation preference set forth in this Regulation 37.1, then such assets (or consideration) shall be distributed among the

holders of the Series B Preferred Shares at the time outstanding, ratably in proportion to the full amounts to which they would otherwise be respectively entitled.

37.2. After the payment of the full liquidation preference of the Series B Preferred Shares as set forth in Regulation 37.1 above, before any distribution or payment shall be made to the holders of any Ordinary Shares, subject to the right of any of the Series A Preferred Shares that may from time to time come into existence, the holders of the Series A Preferred Shares shall be entitled to be paid out of the remaining assets of the Company legally available for distribution in such Liquidation Event (or the consideration received by the Company or its shareholders in an Acquisition), if any, for each Series A Preferred Share held by them, an amount per share of one Series A Preferred Share equal to the Series A Original Issue Price plus all declared and unpaid dividends on such Series A Preferred Share. If, upon any such Liquidation Event, the assets of the Company shall be insufficient to make payment in full to all holders of the Series A Preferred Shares of the liquidation preference set forth in this Regulation 37.2, then such assets (or consideration) shall be distributed among the holders of the Series A Preferred Shares at the time outstanding, ratably in proportion to the full amounts to which they would otherwise be respectively entitled.

37.3. After the payment of the full liquidation preference of the Series B Preferred Shares as set forth in Regulation 37.1 above and the Series A Preferred Shares as set forth in Regulation 37.2 above, the remaining assets of the Company legally available for distribution in such Liquidation Event (or the consideration received by the Company or its shareholders in an Acquisition), if any, shall be distributed ratably to the holders of the Ordinary Shares and Series Preferred Shares on an as-if-converted to Ordinary Shares basis until such holders of Series Preferred Shares have received pursuant to Regulation 37.1 and Regulation 37.2 above and this Regulation 37.3 an aggregate amount per share of Series Preferred Shares equal to three times the Applicable Original Issue Price, respectively; thereafter, the remaining assets of the Company legally available for distribution in such Liquidation Event (or the consideration received by the Company or its shareholders in an Acquisition), if any, shall be distributed ratably to the holders of the Ordinary Shares.

37.4. For the avoidance of doubt, an Asset Transfer or Acquisition shall be deemed a Liquidation Event for purposes of this Regulation 37 and the consideration to be received its shareholders in an Acquisition shall be distributed in the manner described in this Regulation 37.

37.5. In any Acquisition or Asset Transfer, if the consideration to be received is securities of a corporation or other property other than cash, its value will be deemed its fair market value as determined in good faith by the Board on the date such determination is made.

37.6. The Company shall not have the power to effect an Acquisition or Asset Transfer unless the definitive agreement for such transaction provides that the consideration payable to the shareholders of the Company in connection therewith shall be allocated among the holders of share capital of the Company in accordance with this Regulation 37.

37.7. Notwithstanding the foregoing, upon any Liquidation Event (including an Acquisition or Asset Transfer), then each holder of Series Preferred Shares shall be entitled to receive, for each share of each series of Series Preferred Shares then held, out of the proceeds available for distribution, the greater of (i) the amount of cash, securities or other property to which such holder would be entitled to receive with respect to such shares in a Liquidation Event pursuant to Regulations 37.1, 37.2 and 37.3 (without giving effect to this Regulation 37.7) or (ii) the amount of cash, securities or other property to which such holder would be entitled to receive in a Liquidation Event with respect to such shares if such shares had been converted to Ordinary Shares immediately prior to such

Liquidation Event, giving effect to this Regulation 37.7 with respect to all series of Series Preferred Shares simultaneously.

37.8. In the event of a Liquidation Event (including an Acquisition or Asset Transfer), if any portion of the consideration payable to the shareholders of the Company is placed into escrow and/or is payable to the shareholders of the Company subject to contingencies, the definitive agreement shall provide that (x) the portion of such consideration that is not placed in escrow and not subject to any contingencies (the "**Initial Consideration**") shall be allocated among the holders of capital shares of the Company in accordance with Regulations 37.1, 37.2, 37.3, and 37.7 as if the Initial Consideration were the only consideration payable in connection with such Acquisition or Asset Transfer and (y) any additional consideration that becomes payable to the shareholders of the Company upon release from escrow or satisfaction of contingencies shall be allocated among the holders of capital shares of the Company in accordance with Regulations 37.1, 37.2, 37.3, and 37.7 after taking into account the previous payment of the Initial Consideration as part of the same transaction.

38. **Optional Provisions**

38.1. Sections 83, 84 and 193 of the Act shall apply to the Company but, subject to that, the provisions set out in this Constitution shall constitute the whole of the regulations applicable to the Company and no other "optional provisions" as defined by section 1007(2) of the Act shall apply to the Company.

38.2. The optional provisions of the Act which shall not apply are:

38.2.1. Section 80 on Liens

38.2.2. Sections 77 & 78 on Calls on Shares

38.2.3. Section 81 on Forfeiture of Shares

38.2.4. Section 65 on Conversion of Shares into Stock

38.2.5. Section 181 (6) on accidental omission to give notice not invalidating a general meeting

38.2.6. Section 182 (5) on adjourning a meeting if the quorum is not present

38.2.7. Section 229 on Directors interests in other companies promoted by the Company

38.2.8. Section 230 on remuneration of Directors acting in their professional capacity

38.2.9. Section 126 on Bonus Issues

38.2.10. Section 1092 on remuneration of Directors

38.2.11. Section 1090 on rotation of Directors

38.2.12. Section 1113 on voting by Directors in respect of certain matters

We, the body corporate whose name and address is subscribed, wish to be formed into a company in pursuance of this Constitution, and we agree to take the number of shares in the capital of the Company set opposite our name.

Names, Addresses and Descriptions of Subscriber	*Number of Shares taken by the Subscriber*
Goodbody Subscriber One Limited,	1
North Wall Quay, Dublin 1	
Private Company Limited By Shares	
Total Shares Taken:	1

Signature in writing of the above subscriber, attested by witness as provided for below

/s/ Sarah Cleary
For and on behalf of Goodbody Subscriber One Limited

Dated the 16th day of June 2015

Witness to the above Signature:

Signature: /s/ Sarah Cleary
Name: Ciaran Lyng
Address: 25-28 North Wall Quay, Dublin 1

COMPANIES ACT 2014

A PUBLIC COMPANY LIMITED BY SHARES

CONSTITUTION

OF

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY

(adopted on [•] 2018)

COMPANIES ACT 2014

A PUBLIC COMPANY LIMITED BY SHARES

MEMORANDUM OF ASSOCIATION

OF

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY

1. The name of the Company is Iterum Therapeutics public limited company.

2. The Company is a public limited company for the purposes of Part 17 of the Companies Act 2014.

3. The objects for which the Company is established are:

   3.1. To carry on the business of a holding company and to coordinate the administration, finances and activities of any subsidiary companies or associated companies, to do all lawful acts and things whatsoever that are necessary or convenient in carrying on the business of such a holding company and in particular to carry on, in all its branches, the business of a management services company, to act as managers and to direct or coordinate the management of other companies or of the business, property and estates of any company or person and to undertake and carry out all such services in connection therewith as may be deemed necessary or appropriate by the Company's board of directors and to exercise its powers as a shareholder of other companies.

   3.2. To carry on the business of a pharmaceuticals company and to research, develop, design, manufacture, produce, supply, buy, sell, distribute, import, export, provide, promote and otherwise deal in pharmaceuticals, active pharmaceutical ingredients and dosage pharmaceuticals and other devices or products of a pharmaceutical, medicinal or healthcare character and to hold intellectual property rights and to do all things usually done by persons carrying on the above mentioned activities or any of them or likely to be required in connection with any such activities.

   3.3. To invest in pharmaceutical and related assets, including, amongst other items, investments in pharmaceutical companies, products, businesses, divisions, technologies, devices, sales force and other marketing capabilities, development projects and related activities, licences, intellectual and similar property rights, premises and equipment, royalty rights and all other assets needed to operate a pharmaceuticals business.

   3.4. To establish, maintain and operate laboratories for the purposes of carrying on chemical, physical and other research in medicine, chemistry, industry or other unrelated or related fields.

   3.5. To invest (including long-term investments in, and acquisitions of, the shares or other securities or ownership interests in other companies) any monies of the Company in such investments and in such manner as may from time to time be determined, and to hold, sell or deal with such investments and generally to purchase, take on lease or in exchange or otherwise acquire any real and personal property and rights or privileges.

   3.6. To develop and turn to account any land acquired by the Company or in which it is interested and in particular by laying out and preparing the same for building purposes, constructing, altering, pulling down, decorating, maintaining, fitting up and improving buildings and conveniences, and by planting, paving, draining, farming, cultivating, letting on building lease or

building agreement and by advancing money to and entering into contracts and arrangements of all kinds with builders, tenants and others.

3.7. To acquire and hold shares and stocks of any class or description, debentures, debenture stocks, bonds, bills, mortgages, obligations, investments, partnership interests, limited partnership interests, trust interests, membership interests and other securities or ownership interests of all descriptions and of any kind issued or guaranteed by any company or undertaking of whatever nature and wheresoever constituted or carrying on business or issued or guaranteed by any government, state, dominion, colony, sovereign ruler, commissioners, trust, public, municipal, local or other authority or body of whatever nature and wheresoever situated and investments, securities and property of all descriptions and of any kind, including real and chattel real estates, mortgages, reversions, assurance policies, contingencies and choses in action.

3.8. To remunerate by cash payments or allotment of shares or securities or other ownership interests (including rights to acquire shares or securities or other ownership interests) of the Company credited as fully paid up or otherwise any person or company for services rendered or to be rendered to the Company or any parent or subsidiary body corporate whether in the conduct or management of its business, or in placing or assisting to place or guaranteeing the placing of any of the shares of the Company's capital, or any debentures or other securities of the Company or in or about the formation or promotion of the Company.

3.9. To purchase for investment property of any tenure and any interest therein, and to make advances upon the security of land or other similar property or any interest therein.

3.10. To acquire by purchase, exchange, lease, fee, farm grant or otherwise, either for an estate in fee simple or for any less estate or other estate or interest, whether immediate or reversionary and whether vested or contingent, any lands, tenements or hereditaments of any tenure, whether subject or not to any charges or encumbrances, and to hold, farm, work and manage and to let, sublet, mortgage or charge land and buildings of any kind, reversions, interests, annuities, life policies, and any other property real or personal, movable or immovable, either absolutely or conditionally, and either subject or not to any mortgage, charge, ground rent or other rents or encumbrances.

3.11. To erect or secure the erection of buildings or other structures of any kind with a view of occupying or letting them or otherwise utilising them and to enter into any contracts or leases and to grant any licences necessary to effect the same.

3.12. To maintain and improve any lands, tenements or hereditaments acquired by the Company or in which the Company is interested, in particular by decorating, maintaining, furnishing, fitting up and improving houses, shops, flats, maisonettes and other buildings and structures and to enter into contracts and arrangements of all kinds with tenants and others.

3.13. To sell, exchange, mortgage (with or without power of sale), assign, turn to account or otherwise dispose of and generally deal with the whole or any part of the property, shares, stocks, securities, estates, rights or undertakings of the Company, real property, chattels real or personal, movable or immovable, either in whole or in part.

3.14. To take part in the management, supervision, or control of the business or operations of any company or undertaking, and for that purpose to appoint and remunerate any directors, accountants, or other experts or agents to act as consultants, supervisors and agents of other companies or undertakings and to provide managerial, advisory, technical, design, purchasing and selling services and any other services deemed appropriate by the Company.

3.15. To make, draw, accept, endorse, negotiate, issue, execute, discount and otherwise deal with bills of exchange, promissory notes, letters of credit, circular notes, and other negotiable or non-negotiable or transferable or non-transferrable instruments.

3.16. To redeem, purchase, or otherwise acquire in any manner permitted by law any shares in the Company's capital or other securities or ownership interests of any kind issued by the Company.

3.17. To guarantee, support or secure whether by personal covenant or by mortgaging or charging all or any part of the undertaking, property and assets (present and future) and uncalled capital of the Company or by both such methods, or by any other method whatsoever, the performance of the obligations of, and the repayment or payment of the principal amounts of and the premiums, interest, dividends and other amounts due on or with respect to any security of any person, firm or company, including any company which is for the time being the Company's holding company (as defined by section 8 of the Companies Act 2014) or subsidiary (as defined by section 7 of the Companies Act 2014) or another subsidiary as defined by the said section of the Company's holding company (as defined by section 8 of the Companies Act 2014) or otherwise associated with the Company in business notwithstanding the fact that the Company may not receive any consideration, advantage or benefit, direct or indirect from entering into such guarantee or other arrangement or transaction contemplated herein.

3.18. To lend the funds of the Company with or without security and at interest or free of interest.

3.19. To raise or borrow or secure the payment of money, including by the issue of bonds, debentures or debenture stock, perpetual or redeemable, or by mortgage, charge, lien or pledge upon the whole or any part of the undertaking, property, assets or rights of the Company, present or future, including its uncalled capital and generally in any other manner as the directors shall from time to time determine and to enter into or issue interest and currency hedging and swap agreements, forward rate agreements, interest and currency futures or options and other forms of financial instruments, and to purchase, redeem or pay off any of the foregoing and to guarantee any or all of the liabilities of the Company, any other company or any other person, and any debentures, debenture stock or other securities may be issued at a discount, premium or otherwise, and with any special privileges as to redemption, surrender, transfer, drawings, allotments of shares, attending and voting at general meetings of the Company, appointment of directors and otherwise.

3.20. To accumulate capital for any of the purposes of the Company, and to appropriate any of the Company's assets to specific purposes, either conditionally or unconditionally, and to admit any class or section of those who have any dealings with the Company to any share in the profits thereof or in the profits of any particular branch of the Company's business or to any other special rights, privileges, advantages or benefits.

3.21. To reduce the share capital of the Company in any manner permitted by law.

3.22. To make gifts or grant bonuses to officers or other persons who are or have been in the employment of the Company and to allow any such persons to have the use and enjoyment of such property, chattels or other assets belonging to the Company upon such terms as the Company shall think fit.

3.23. To establish and maintain or procure the establishment and maintenance of any pension or superannuation fund (whether contributory or otherwise) for the benefit of and to give or procure the giving of donations, gratuities, pensions, annuities, allowances, emoluments or charitable aid to any persons who are or were at any time in the employment or service of the Company or any of its predecessors in business, or of any company which is a subsidiary of the Company or who may be or have been directors or officers of the Company, or of any such other company as aforesaid, or any persons in whose welfare the Company or any such other

company as aforesaid may be interested and the wives, husbands, widows, widowers, families, relatives or dependants of any such persons, and to make payments towards insurance and assurance and to form and contribute to provident and benefit funds for the benefit of any such persons and to remunerate any person, firm or company rendering services to the Company or of any company which is a subsidiary of the Company, whether by cash payment, gratuities, pensions, annuities, allowances, emoluments or by the allotment of shares or securities of the Company credited as paid up in full or in part or otherwise.

3.24. To employ experts to investigate and examine into the conditions, prospects, value, character and circumstances of any business concerns, undertakings, assets, property or rights.

3.25. To insure the life of any person who may, in the opinion of the Company, be of value to the Company, as having or holding for the Company interests, goodwill, or influence or otherwise and to pay the premiums on such insurance.

3.26. To distribute either upon a distribution of assets or division of profits among the Members of the Company in kind any property of the Company, and in particular any shares, debentures or securities of other companies belonging to the Company or of which the Company may have the power of disposing.

3.27. To give, whether directly or indirectly, and whether by means of a loan, guarantee, the provision of security or otherwise, any financial assistance for the purpose of or in connection with a purchase or subscription made or to be made by any person of or for any shares in the Company, or, where the Company is a subsidiary company, in its holding company.

3.28. To do and carry out all or any of the foregoing or following objects in any part of the world and either as principals, agents, contractors, trustees or otherwise, and either by or through agents, trustees or otherwise and either alone or in partnership or in conjunction with any other company, firm or person, provided that nothing herein contained shall empower the Company to carry on the business of insurance.

3.29. To apply for, purchase or otherwise acquire any patents, brevets d'invention, licences, trademarks, trade names, copyrights, industrial designs, know-how, concessions and other forms of intellectual property rights and the like conferring any exclusive or non-exclusive or limited or contingent rights to use, or any secret or other information as to any invention or process of the Company, or the acquisition of which may seem calculated directly or indirectly to benefit the Company, and to use, exercise, develop, or grant licences in respect of, or otherwise turn to account the property, rights or information so acquired.

3.30. To enter into partnership or into any arrangement for sharing profits, union of interests, co-operation, joint venture, reciprocal concession or otherwise with any person or company.

3.31. To acquire and undertake the whole or any part of the undertaking, business, property and liabilities of any person or company.

3.32. To adopt such means of making known the Company and its products and services as may seem expedient.

3.33. To acquire and carry on any business carried on by a subsidiary or a holding company of the Company or another subsidiary of a holding company of the Company.

3.34. To promote any company or companies for the purpose of acquiring all or any of the property and liabilities of this Company or for any other purpose which may seem directly or indirectly calculated to benefit this Company.

3.35. To amalgamate with, merge with or otherwise become part of or associated with any other company or association in any manner permitted by law.

3.36. To make voluntary dispositions of all or any part of the property and rights of the Company and to make gifts thereof or gratuitous payments either for no consideration or for a consideration less than the market value of such property or rights or the amount of cash payment or by all or any such methods.

3.37. To receive voluntary dispositions of all or any part of the undertakings, properties, assets or rights of any other corporation and to receive gifts thereof or gratuitous payments either for no consideration or for a consideration less than the market value of such property or rights or the amount of cash payment or by all or any such methods.

3.38. To do and carry out all such other things, except the issuing of policies of insurance, as may be deemed by the Company capable of being carried on in connection with the above objects or any of them or calculated to enhance the value of or render profitable any of the Company's undertakings, properties, assets or rights.

And it is hereby declared that (i) the word "company" in this clause, except where used in reference to this Company, shall be deemed to include any person, partnership, limited partnership, limited liability partnership, limited liability company, other corporate body, trust or other body of persons whether incorporated or not incorporated and whether domiciled in Ireland or elsewhere and that the objects of the Company as specified in each of the foregoing paragraphs of this clause shall be separate and distinct objects and shall not be in anyway limited or restricted by reference to or inference from the terms of any other paragraph or the name of the Company and (ii) any phrase introduced by the terms "including", "include", "in particular" or any similar expression shall be construed as illustrative and shall not limit the sense of the words preceding those terms.

4. The liability of each Member is limited to the amount from time to time unpaid on such Member's Shares.

5. The authorised share capital of the Company is US$1,500,000 divided into 50,000,000 Ordinary Shares of US$0.01 each and 100,000,000 Preferred Shares of US$0.01 each.

6. The shares forming the capital, increased or reduced, may be increased or reduced and be divided into such classes and issued with any special rights, privileges and conditions or with such qualifications as regards preference, dividend, capital, voting or other special incidents, and be held upon such terms as may be attached thereto or as may from time to time be provided by the original or any substituted or amended Articles of Association and regulations of the Company for the time being, but so that where shares are issued with any preferential or special rights attached thereto such rights shall not be alterable otherwise than pursuant to the provisions of the Company's Articles of Association for the time being.

7. Capitalised terms that are not defined in this Memorandum of Association bear the same meaning as those given in the Articles of Association of the Company.

COMPANIES ACT 2014

A PUBLIC COMPANY LIMITED BY SHARES

ARTICLES OF ASSOCIATION

OF

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY

TABLE OF CONTENTS

PRELIMINARY	9
REGISTERED OFFICE	12
SHARE CAPITAL; ISSUE OF SHARES	13
ORDINARY SHARES	14
PREFERRED SHARES	14
ISSUE OF WARRANTS	15
CERTIFICATES FOR SHARES	15
REGISTER OF MEMBERS	15
TRANSFER OF SHARES	16
REDEMPTION AND REPURCHASE OF SHARES	18
VARIATION OF RIGHTS OF SHARES	18
LIEN ON SHARES	19
CALLS ON SHARES	20
FORFEITURE	21
NON-RECOGNITION OF TRUSTS	22
TRANSMISSION OF SHARES	22
AMENDMENT OF MEMORANDUM OF ASSOCIATION; CHANGE OF LOCATION OF REGISTERED OFFICE; AND ALTERATION OF CAPITAL	23
CLOSING REGISTER OF MEMBERS OR FIXING RECORD DATE	24
GENERAL MEETINGS	25
NOTICE OF GENERAL MEETINGS	25
PROCEEDINGS AT GENERAL MEETINGS	26
VOTES OF MEMBERS	30
PROXIES AND CORPORATE REPRESENTATIVES	30
DIRECTORS	32
DIRECTORS' AND OFFICERS' INTERESTS	32
POWERS AND DUTIES OF DIRECTORS	34

MINUTES 35
DELEGATION OF THE BOARD'S POWERS 35
CHAIRPERSON AND EXECUTIVE OFFICERS 36
PROCEEDINGS OF DIRECTORS 36
RESIGNATION AND DISQUALIFICATION OF DIRECTORS 37
APPOINTMENT, ROTATION AND NOMINATION OF DIRECTORS 38
SECRETARY 40
SEAL 40
DIVIDENDS, DISTRIBUTIONS AND RESERVES 41
CAPITALISATION 42
ACCOUNTS 42
AUDIT 43
NOTICES 43
UNTRACED HOLDERS 45
DESTRUCTION OF DOCUMENTS 46
WINDING UP 47
INDEMNITY 47
FINANCIAL YEAR 49
SHAREHOLDER RIGHTS PLAN 49
BUSINESS COMBINATION 49

1. Sections 43(2), 43(3), 65(2)-(7), 77-81, 83(3), 94(1), 95(1), 96(2)-(11), 124, 125, 126(2) to (8), 144(3)-(4), 148(2), 158-165, 178(2), 180(5), 181(1), 181(6), 182(2), 182(5), 183(3), 186(c)(i), 187, 188, 193, 218(3)-(5), 229, 230, 338(5)-(6), 618(1)(b), 620(8), 1090, 1092, and 1113 of the Companies Act shall not apply to the Company. The provisions of the Companies Act which are stated therein to apply to a public limited company, save to the extent that its constitution is permitted to provide or state otherwise, will apply to the Company subject to the alterations contained in these Articles, and will, so far as not inconsistent with these Articles, bind the Company and its Members.

2.

2.1. In these Articles:

"1990 Regulations"	The Companies Act 1990 (Uncertificated Securities) Regulations 1996 (S.I. No. 68 of 1996) as may be amended from time to time.
"address"	includes any number or address used for the purposes of communication by way of electronic mail or other electronic communication.
"Adoption Date"	means [•] 2018.
"Articles" or **"Articles of Association"**	means these articles of association of the Company, as amended from time to time by Special Resolution.
"Assistant Secretary"	means any person appointed by the Board from time to time to assist the Secretary.
"Auditors"	means the persons for the time being performing the duties of the statutory auditors of the Company.
"Board"	means the board of Directors for the time being of the Company.
"Chairperson"	means the chairperson of the Board from time to time and/or chairperson of a general meeting of the Company as the context may require.
"clear days"	means, in relation to a period of notice, that period excluding the day when the notice is given or deemed to be given and the day for which notice is being given or on which an action or event for which notice is being given is to occur or take effect.
"Companies Act"	means the Companies Act 2014 and every statutory modification, replacement and re-enactment thereof for the

	time being in force.
"Company"	means Iterum Therapeutics plc.
"Court"	means the Irish High Court.
"Derivative Transaction"	means any agreement, arrangement, interest or understanding entered into by, or on behalf or for the benefit of, any Proponent or any of its affiliates or associates, whether record or beneficial: (A) the value of which is derived in whole or in part from the value of any class or series of shares or other securities of the Company, (B) which otherwise provides any direct or indirect opportunity to gain or share in any gain derived from a change in the value of securities of the Company, (C) the effect or intent of which is to mitigate loss, manage risk or benefit of security value or price changes with respect to any securities of the Company, or (D) which provides the right to vote or increase or decrease the voting power of, such Proponent, or any of its affiliates or associates, with respect to any securities of the Company, which agreement, arrangement, interest or understanding may include, without limitation, any option, warrant, debt position, note, bond, convertible security, swap, stock appreciation right, short position, profit interest, hedge, right to dividends, voting agreement, performance-related fee or arrangement to borrow or lend shares (whether or not subject to payment, settlement, exercise or conversion in any such class or series), and any proportionate interest of such Proponent in the securities of the Company held by any general or limited partnership, or any limited liability company, of which such Proponent is, directly or indirectly, a general partner or managing member.
"Directors"	means the directors for the time being of the Company.
"dividend"	includes dividends, final dividends, interim dividends and bonus dividends.
"electronic communication"	shall have the meaning given to those words in the Electronic Commerce Act 2000.
"electronic signature"	shall have the meaning given to those words in the Electronic Commerce Act 2000.
"Enterprise"	means the Company and any other corporation, limited liability company, partnership, joint venture, trust, employee benefit plan or other enterprise or entity which a person is

	or was serving at the request of the Company;
"Exchange"	means any securities exchange or other system on which the Shares of the Company may be listed or otherwise authorised for trading from time to time.
"Exchange Act"	means the Securities Exchange Act of 1934 of the United States of America.
"Member"	means a person who has agreed to become a member of the Company and whose name is entered in the Register of Members as a registered holder of Shares.
"Memorandum"	means the memorandum of association of the Company as amended from time to time by Special Resolution.
"month"	means a calendar month.
"Official"	means a director, officer, secretary, employee, trustee, agent, partner, managing member, fiduciary or other official of the Company or another Enterprise;
"Ordinary Resolution"	means an ordinary resolution of the Company's Members within the meaning of section 191 of the Companies Act.
"paid-up"	means paid-up in accordance with the Companies Act as to the nominal value and any premium payable in respect of the issue of any Shares and includes credited as paid-up.
"Redeemable Shares"	means redeemable shares in accordance with the Companies Act.
"Register of Members" or **"Register"**	means the register of Members of the Company maintained by or on behalf of the Company, in accordance with the Companies Act.
"registered office"	means the registered office for the time being of the Company.
"Seal"	means the seal of the Company, if any, and includes every duplicate seal.
"Secretary"	means the person appointed by the Board to perform any or all of the duties of secretary of the Company and includes an Assistant Secretary and any person appointed by the Board or the Secretary to perform the duties of secretary of

	the Company, in each case, when acting in the capacity of the secretary of the Company.
"Share" and "Shares"	means a share or shares in the capital of the Company.
"Special Resolution"	means a special resolution of the Company's Members within the meaning of section 191 of the Companies Act.

2.2. In these Articles (unless otherwise specified):

2.2.1. words importing the singular number include the plural number and vice-versa;

2.2.2. words importing the feminine gender include the masculine gender and the neuter and vice-versa;

2.2.3. words importing persons include any company, partnership or other body of persons, whether corporate or not, any trust and any government, governmental body or agency or public authority, whether of Ireland or elsewhere and references to a company, except where used in reference to the Company, shall be deemed to include any person, partnership, limited partnership, limited liability partnership, limited liability company, other corporate body, trust or other body of persons whether incorporated or not incorporated and whether domiciled in Ireland or elsewhere;

2.2.4. expressions referring to "written" and "in writing" shall be construed, unless the contrary intention appears, as including references to printing, lithography, photography and any other modes of representing or reproducing words in a visible form except as provided in these Articles and/or where it constitutes writing in electronic form sent to the Company;

2.2.5. expressions referring to execution of any document shall include any mode of execution whether under seal or under hand or any mode of electronic signature;

2.2.6. references to provisions of any law or regulation shall be construed as references to those provisions as amended, modified, re-enacted or replaced from time to time;

2.2.7. any phrase introduced by the terms "including", "include", "in particular" or any similar expression shall be construed as illustrative and shall not limit the sense of the words preceding those terms;

2.2.8. reference to "officer" or "officers" in these Articles means any executive that has been designated by the Company as an "officer" and, for the avoidance of doubt, shall not have the meaning given to such term in the Companies Act and any such officers shall not constitute officers of the Company within the meaning of section 2(1) of the Companies Act;

2.2.9. headings are inserted for reference only and shall be ignored in construing these Articles; and

2.2.10. references to US$, USD, $ or dollars shall mean United States dollars, the lawful currency of the United States of America and references to €, euro, or EUR shall mean the euro, the lawful currency of Ireland.

REGISTERED OFFICE

3. The registered office shall be at such place in Ireland as the Board from time to time shall decide.

SHARE CAPITAL; ISSUE OF SHARES

4. The authorised share capital of the Company is US$1,500,000 divided into 50,000,000 Ordinary Shares of US$0.01 each and 100,000,000 Preferred Shares of US$0.01 each.

5. Subject to the provisions of these Articles relating to new Shares, the Shares shall be at the disposal of the Directors, and they may (subject to the provisions of the Companies Act) allot, issue, grant options over or otherwise dispose of them to such persons, on such terms and conditions and at such times as they may consider to be in the best interests of the Company and its Members, but so that no Share shall be issued at a discount save in accordance with sections 71(4) and 1026 of the Companies Act, and so that, in the case of Shares offered to the public for subscription, the amount payable on application on each such Share shall not be less than one-quarter of the nominal amount of the Share and the whole of any premium thereon. To the extent permitted by the Companies Act, Shares may also be allotted by a committee of the Directors or by any other person where such committee or person is so authorised by the Directors.

6. Subject to any requirement to obtain the approval of Members under any laws, regulations or the rules of any Exchange, the Board is authorised, from time to time, to grant such persons, for such periods and upon such terms as the Board deems advisable, options or awards to purchase or subscribe for any number of Shares of any class or classes or of any series of any class and other securities or ownership interests of the Company as the Board may deem advisable, and to cause warrants or other appropriate instruments evidencing such options or awards to be issued.

7.

7.1. The Directors are, for the purposes of section 1021 of the Companies Act, generally and unconditionally authorised to exercise all powers of the Company to allot and issue relevant securities (as defined by the said section 1021) up to the amount of the Company's authorised but unissued share capital as at the Adoption Date and to allot and issue any Shares acquired by or on behalf of the Company pursuant to the provisions of the Companies Act and held as treasury shares and, unless it is renewed or a longer period of time is allowed under applicable law, this authority shall expire five years from the Adoption Date.

7.2. The Directors are hereby empowered pursuant to sections 1022 and 1023(3) of the Companies Act to allot equity securities within the meaning of the said section 1023 for cash pursuant to the authority conferred by Article 7.1 as if section 1022 of the Companies Act did not apply to any such allotment.

7.3. The Company may before the expiry of the authorities conferred by Articles 7.1 and/or 7.2 make an offer or agreement which would or might require relevant securities (as defined in section 1021 of the Companies Act) and/or equity securities (as defined in section 1023 of the Companies Act), as the case may be, to be allotted after such expiry and the Board may allot relevant securities and/or equity securities in pursuance of such an offer or agreement as if the authorities conferred by Articles 7.1 and/or 7.2 had not expired.

7.4. The Company may issue permissible letters of allotment (as defined by section 1019 of the Companies Act) to the extent permitted by the Companies Act.

8. The Company may pay commission to any person in consideration of any person subscribing or agreeing to subscribe, whether absolutely or conditionally, for the Shares in the Company or procuring or agreeing to procure subscriptions, whether absolute or conditional, for any Shares in the Company on such terms and, subject to the provisions of the Companies Act and to such conditions as the Board may determine including by paying cash or allotting and issuing fully or partly paid Shares or any combination of the two. The Company may also on any issue of Shares pay such brokerage as may be

lawful.

ORDINARY SHARES

9. The rights and restrictions attaching to the Ordinary Shares shall be as follows:

   9.1. subject to the right of the Company to set record dates for the purposes of determining the identity of Members entitled to notice of and/or to vote at a general meeting and any rules or regulations applicable to the conduct of any general meeting of the Company, the right to attend and speak at any general meeting of the Company and to exercise one vote per Ordinary Share held at any general meeting of the Company;

   9.2. the right to participate pro rata in all dividends declared by the Company with respect to the Ordinary Shares; and

   9.3. the right, in the event of the Company's winding up, to participate pro rata with all other Ordinary Shares in the total assets of the Company.

10. The rights attaching to the Ordinary Shares shall be subject to the terms of issue of any series or class of Preferred Shares allotted by the Directors from time to time in accordance with Article 13.

11. Unless the Board specifically resolves to treat such acquisition as a purchase for the purposes of the Companies Act, an Ordinary Share shall be deemed to be a Redeemable Share on, and from the time of, the existence or creation of an agreement, transaction or trade between the Company (including any agent or broker acting on behalf of the Company) and any third party pursuant to which the Company acquires or will acquire Ordinary Shares, or an interest in Ordinary Shares, from such third party and the Company is hereby authorised to enter into any such agreement, transaction or trade. In these circumstances, the acquisition of such shares or interest in shares by the Company shall constitute the redemption of a Redeemable Share in accordance with the Companies Act. No resolution, whether special or otherwise, shall be required to be passed to deem any Ordinary Share a Redeemable Share, or to authorise the redemption of such a Redeemable Share and once deemed to be a Redeemable Share such share shall be redeemable at the instance of the Company.

12. All Ordinary Shares shall rank *pari passu* with each other in all respects.

PREFERRED SHARES

13. The Directors are authorised to issue all or any of the authorised but unissued Preferred Shares from time to time in one or more classes or series, and to fix for each such class or series such voting power, full or limited, or no voting power, and such designations, preferences and relative, participating, optional or other special rights and such qualifications, limitations or restrictions thereof, as shall be stated and expressed in the resolution or resolutions adopted by the Directors providing for the issuance of such class or series, including (but not limited to) the authority to provide that any such class or series may be:

   13.1. redeemable at the option of the Company, or the holders, or both, with the manner of the redemption to be set by the Directors, and redeemable at such time or times, including upon a fixed date, and at such price or prices as the Directors may determine;

   13.2. entitled to receive dividends (which may be cumulative or non-cumulative) at such rates, on such conditions and at such times as the Directors may determine, and which may be payable in preference to, or in such relation to, the dividends payable on any other class or classes of Shares or any other series as the Directors may determine;

   13.3. entitled to such rights upon the dissolution of, or upon any distribution of the assets of, the Company as the Directors may determine; or

13.4. convertible into, or exchangeable for, Shares of any other class or classes of Shares, or of any other series of the same or any other class or classes of Shares, of the Company at such price or prices or at such rates of exchange and with such adjustments as the Directors may determine.

The Directors may at any time before the allotment of any Preferred Share by further resolution in any way amend the designations, preferences, rights, qualifications, limitations or restrictions, or vary or revoke the designations of such Preferred Shares.

14. The rights conferred upon the holder of any pre-existing Shares in the share capital of the Company shall be deemed not to be varied by the creation, issue and allotment of Preferred Shares in accordance with Article 13.

ISSUE OF WARRANTS

15. The Board may issue warrants to subscribe for any class of Shares or other securities of the Company on such terms as it may from time to time determine.

CERTIFICATES FOR SHARES

16. Unless otherwise provided for by the Board or the rights attaching to or by the terms of issue of any particular Shares, or to the extent required by any Exchange, depository or any operator of any clearance or settlement system or by law, no person whose name is entered as a Member in the Register of Members shall be entitled to receive a share certificate for any Shares of any class held by him or her (nor on transferring a part of holding, to a certificate for the balance).

17. Any share certificate, if issued, shall specify the number of Shares in respect of which it is issued and the amount paid thereon or the fact that they are fully paid, as the case may be, and may otherwise be in such form as shall be determined by the Board. Such certificates may be under Seal. All certificates for Shares shall be consecutively numbered or otherwise identified and shall specify the Shares to which they relate. The name and address of the person to whom the Shares represented thereby are issued, with the number of Shares and date of issue, shall be entered in the Register of Members. All certificates surrendered to the Company for transfer shall be cancelled and no new certificate shall be issued until the former certificate for a like number of Shares shall have been surrendered and cancelled. The Board may authorise certificates to be issued with the Seal and authorised signature(s) affixed by some method or system of mechanical or electronic process. In respect of a Share or Shares held jointly by several persons, the Company shall not be bound to issue a certificate or certificates to each such person, and the issue and delivery of a certificate or certificates to one of several joint holders shall be sufficient delivery to all such holders.

18. If a share certificate is defaced, worn out, lost or destroyed, it may be renewed on such terms (if any) as to evidence and indemnity and on the payment of such expenses reasonably incurred by the Company in investigating such evidence, as the Board may prescribe, and, in the case of defacement or wearing out, upon delivery of the old certificate.

REGISTER OF MEMBERS

19. The Company shall maintain or cause to be maintained a Register of its Members in accordance with the Companies Act.

20. If the Board considers it necessary or appropriate, the Company may establish and maintain a duplicate Register or Registers of Members at such location or locations within or outside Ireland as the Board thinks fit. The original Register of Members shall be treated as the Register of Members for the purposes of these Articles and the Companies Act.

21. The Company, or any agent(s) appointed by it to maintain any duplicate Register of Members in accordance with these Articles shall, as soon as practicable and on a regular basis record, or procure the recording of, in the original Register of Members, all transfers of Shares effected on any duplicate Register of Members and shall at all times maintain the original Register of Members in such manner as to show at all times the Members for the time being and the Shares respectively held by them, in all respects in accordance with the Companies Act.

22. The Company shall not be bound to register more than four (4) persons as joint holders of any Share. If any Share shall stand in the names of two (2) or more persons, the person first named in the Register of Members shall be deemed the sole holder thereof as regards service of notices and, subject to the provisions of these Articles, all or any other matters connected with the Company.

TRANSFER OF SHARES

23. Subject to such of the restrictions of these Articles and to such of the conditions of issue or transfer as may be applicable, all transfers of Shares shall be effected by an instrument in writing (an "**instrument of transfer**") in such form as the Board or the Secretary may approve. All such instruments of transfer must be left at the registered office or at such other place as the Board or the Secretary may specify and all such instruments of transfer shall be retained by the Company.

24.

24.1. In the case of transfers to Cede & Co (or to any successor thereto, or to any other affiliate or nominee of The Depositary Trust Company or of any successor to The Depositary Trust Company) the instrument of transfer shall not be effective until executed by:

24.1.1. the Secretary (or such person as may be nominated by the Secretary for this purpose) on behalf of the Company; and

24.1.2. by the transferor or alternatively by or on behalf of the transferor by the Secretary (or such person as may be nominated by the Secretary for this purpose) on behalf of the Company, and the Company shall be deemed to have been irrevocably appointed agent for the transferor of such Share or Shares with full power to execute, complete and deliver in the name of and on behalf of the transferor of such Share or Shares all such transfers of Shares held by the Members in the share capital of the Company.

24.2. In the case of transfers other than those to Cede & Co (or to any successor thereto, or to any other affiliate or nominee of The Depositary Trust Company or of any successor to The Depositary Trust Company), the instrument of transfer of any Share shall be executed by the transferor or alternatively for and on behalf of the transferor by the Secretary (or such other person as may be nominated by the Secretary for this purpose) on behalf of the Company, and the Secretary (or relevant nominee), acting on behalf of the Company shall be deemed to have been irrevocably appointed agent for the transferor of such Share or Shares with full power to execute, complete and deliver in the name of and on behalf of the transferor of such Share or Shares all such transfers of Shares held by the Members in the share capital of the Company.

24.3. An instrument of transfer need not be executed by the transferee except to the extent required by the Companies Act. Any document which records the name of the transferor, the name of the transferee, the class and number of Shares agreed to be transferred and the date of the agreement to transfer the Shares, shall, once executed in accordance with this Article, be deemed to be a proper instrument of transfer for the purposes of section 94 of the Companies Act.

24.4. The transferor shall be deemed to remain the holder of the Share until the name of the transferee is entered on the Register in respect thereof, and neither the title of the transferee

nor the title of the transferor shall be affected by any irregularity or invalidity in the proceedings in reference to the sale should the Board so determine.

24.5. The Company, at its absolute discretion and insofar as the Companies Act or any other applicable law permits, may, or may procure that a subsidiary of the Company shall, pay Irish stamp duty arising on a transfer of Shares on behalf of the transferor or transferee of such Shares of the Company. If stamp duty resulting from the transfer of Shares in the Company which would otherwise be payable by the transferor or transferee is paid by the Company or any subsidiary of the Company on behalf of the transferor or transferee, then in those circumstances, the Company shall, on its behalf or on behalf of its subsidiary (as the case may be), be entitled, but not required, to (i) seek reimbursement of the stamp duty from the transferor or transferee, (ii) set-off the stamp duty against any dividends payable to the transferor or transferee of those Shares or (iii) claim a first and permanent lien on the Shares on which stamp duty has been paid by the Company or its subsidiary for the amount of stamp duty paid.

24.6. Notwithstanding the provisions of these Articles and subject to any regulations made under section 1086 of the Companies Act or the 1990 Regulations (including any modification thereof or any regulations in substitution therefor made under the Companies Act or otherwise), title to any Shares in the Company may also be evidenced and transferred without a written instrument in accordance with section 1086 of the Companies Act or any regulations made thereunder or the 1990 Regulations (including any modification thereof or any regulations in substitution therefor made under the Companies Act or otherwise). The Board shall have power to permit any class of Shares to be held in uncertificated form and to implement any arrangements they think fit for such evidencing and transfer which accord with such regulations and in particular shall, where appropriate, be entitled to disapply or modify all or part of the provisions in these Articles with respect to the requirement for written instruments of transfer and share certificates (if any), in order to give effect to such regulations.

25. The Board may, without assigning any reason for its decision, decline to register any transfer of any Share which is not a fully paid Share. The Board may also, without assigning any reason, refuse to register a transfer of any Share unless:

25.1. the instrument of transfer is fully and properly completed and is lodged with the Company at the registered office or at such other place as the Board or the Secretary may specify accompanied by the certificate(s) for the Shares (if any) to which it relates (which shall upon registration of the transfer be cancelled) and such other evidence as the Board may reasonably require to show the right of the transferor to make the transfer;

25.2. the instrument of transfer is in respect of only one class of Shares;

25.3. a registration statement under the Securities Act of 1933 (as amended) of the United States of America is in effect with respect to such transfer or such transfer is exempt from registration and, if requested by the Board, a written opinion from counsel reasonably acceptable to the Board is obtained to the effect that such transfer is exempt from registration;

25.4. the instrument of transfer is properly stamped (in circumstances where stamping is required);

25.5. in the case of a transfer to joint holders, the number of joint holders to which the Share is to be transferred does not exceed four;

25.6. it is satisfied, acting reasonably, that all applicable consents, authorisations, permissions or approvals of any governmental body or agency in Ireland or any other applicable jurisdiction required to be obtained under relevant law prior to such transfer have been obtained; and

25.7. it is satisfied, acting reasonably, that the transfer would not violate the terms of any agreement to which the Company (or any of its subsidiaries) and the transferor are party or subject.

26. If the Board shall refuse to register a transfer of any Share, it shall, within two (2) months after the date on which the transfer was lodged with the Company, send to each of the transferor and the transferee notice of such refusal.

27. The Company shall not be obligated to make any transfer to an individual under 18 years of age or to a person in respect of whom an order has been made by a competent court or official on the grounds that he or she is or may be suffering from mental disorder or is otherwise incapable of managing his or her affairs or under other legal disability.

28. Upon every transfer of Shares, the certificate (if any) held by the transferor shall be given up to be cancelled, and shall forthwith be cancelled accordingly, and subject to Article 16 a new certificate may be issued without charge to the transferee in respect of the Shares transferred to him or her, and if any of the Shares included in the certificate so given up shall be retained by the transferor, a new certificate in respect thereof may be issued to him or her without charge.

REDEMPTION AND REPURCHASE OF SHARES

29. Subject to the provisions of Chapter 6 of Part 3 and Chapter 5 of Part 17 of the Companies Act and the other provisions of this Article 29, and without prejudice to Article 13, the Company may:

29.1. pursuant to section 66(4) of the Companies Act, allot and issue any Shares of the Company which are to be redeemed or are liable to be redeemed at the option of the Company or the Member on such terms and in such manner as may be determined by the Board;

29.2. redeem Shares of the Company on such terms as may be contained in, or be determined pursuant to the provisions of, these Articles. Subject as aforesaid, the Company may cancel any Shares so redeemed or may hold them as treasury shares (as defined by section 106(1) of the Companies Act) and re-issue such treasury shares as Shares of any class or classes or cancel them;

29.3. subject to or in accordance with the provisions of the Companies Act and without prejudice to any relevant special rights attached to any class of Shares, pursuant to section 105 and Chapter 5 of Part 17 of the Companies Act, acquire any of its own Shares (including any Redeemable Shares and without any obligation to acquire on any *pro rata* basis as between Members or Members of the same class) and may cancel any Shares so acquired or hold them as treasury shares (as defined by section 106(1) of the Companies Act) and may re-issue any such Shares as Shares of any class or classes or cancel them; or

29.4. convert any of its Shares into Redeemable Shares provided that the total number of Shares which shall be redeemable pursuant to this authority shall not exceed the limit in section 1071(b) of the Companies Act. No resolution of Members, whether special or otherwise, shall be required to be passed to convert any of the Company's Shares into Redeemable Shares.

30. The Company may make a payment in respect of the redemption or purchase of its own Shares in any manner permitted by the Companies Act.

31. The holder of the Shares being redeemed or purchased shall be bound to deliver up to the Company, at its registered office or such other place as the Board shall specify, the certificate(s) (if any) thereof for cancellation and thereupon the Company shall pay to him or her the purchase or redemption monies or consideration in respect thereof.

VARIATION OF RIGHTS OF SHARES

32. Without prejudice to the authority conferred on the Directors pursuant to Article 13 to issue Preferred Shares in the capital of the Company, if at any time the share capital of the Company is divided into different classes or series of Shares, the rights attached to any class or series (unless otherwise provided by the terms of issue of the Shares of that class or series) may be varied or abrogated with the consent in writing of the holders of a majority of the issued Shares of that class or series entitled to vote on such variation or abrogation, or with the sanction of an Ordinary Resolution passed at a general meeting of the holders of the Shares of that class or series.

33. The provisions of these Articles relating to general meetings of the Company shall apply *mutatis mutandis* to every such general meeting of the holders of one class or series of Shares except that the necessary quorum shall be one or more persons holding or representing by proxy at least a majority of the issued Shares of the class or series.

34. The rights conferred upon the holders of the Shares of any class or series issued with preferred or other rights shall not, unless otherwise expressly provided by the terms of issue of the Shares of that class or series, be deemed to be varied by (i) the creation or issue of further Shares ranking *pari passu* therewith; (ii) a purchase or redemption by the Company of its own Shares; or (iii) the creation or issue for value (as determined by the Board) of further Shares ranking as regards participation in the profits or assets of the Company or otherwise in priority to them. For the avoidance of doubt:

    34.1. the issue, redemption or purchase of any of the 100,000,000 Preferred Shares of US$0.01 each shall not constitute a variation of the rights of the holders of Ordinary Shares; and

    34.2. the issue of Preferred Shares or any class or series of Preferred Shares which rank *pari passu* with, or junior to, any existing Preferred Shares or class or series of Preferred Shares shall not constitute a variation of the existing Preferred Shares or class or series of Preferred Shares.

LIEN ON SHARES

35. The Company shall have a first and paramount lien on every Share (not being a fully paid Share) for all monies (whether presently payable or not) payable at a fixed time or called in respect of that Share. The Board, at any time, may declare any Share to be wholly or in part exempt from the provisions of this Article 35. The Company's lien on a Share shall extend to all monies payable in respect of it.

36. The Company may sell in such manner as the Board determines any Share on which the Company has a lien if a sum in respect of which the lien exists is presently payable and is not paid within fourteen (14) clear days after notice demanding payment, stating that if the notice is not complied with the Share may be sold, has been given to the holder of the Share or to the person entitled to it by reason of the death, bankruptcy or insolvency of the holder or otherwise by operation of law or regulation (whether of Ireland or otherwise).

37. To give effect to a sale, the Board may authorise some person to execute an instrument of transfer of the Share(s) sold to, or in accordance with, the directions of the transferee. The transferee shall be entered in the Register as the holder of the Share(s) comprised in any such transfer and he or she shall not be bound to see to the application of the purchase monies nor shall his or her title to the Share be affected by any irregularity in, or invalidity of, the proceedings in reference to the sale, and after the name of the transferee has been entered in the Register, the remedy of any person aggrieved by the sale shall be in damages only and against the Company exclusively.

38. The net proceeds of the sale, after payment of the costs, shall be applied in payment of so much of the sum for which the lien exists as is presently payable and any residue (upon surrender to the Company for cancellation of the certificate for the Shares sold and subject to a like lien for any monies not presently payable as existed upon the Shares before the sale) shall be paid to the person entitled to the Shares at the date of the sale.

39. Whenever any law for the time being of any country, state or place imposes or purports to impose any immediate or future or possible liability upon the Company to make any payment or empowers any government or taxing authority or government official to require the Company to make any payment in respect of any Shares registered in the Register as held either jointly or solely by any Members or in respect of any dividends, bonuses or other monies due or payable or accruing due or which may become due or payable to such Member by the Company on, or in respect of, any Shares registered as mentioned above or for or on account or in respect of any Member and whether in consequence of:

(a) the death of such Member;

(b) the non-payment of any income tax or other tax by such Member;

(c) the non-payment of any estate, probate, succession, death, stamp or other duty by the executor or administrator of such Member or by or out of his or her estate; or

(d) any other act or thing;

in every such case (except to the extent that the rights conferred upon holders of any class of Shares renders the Company liable to make additional payments in respect of sums withheld on account of the foregoing):

39.1. the Company shall be fully indemnified by such Member or his or her executor or administrator from all liability;

39.2. the Company shall have a lien upon all dividends and other monies payable in respect of the Shares registered in the Register as held either jointly or solely by such Member for all monies paid or payable by the Company as referred to above in respect of such Shares or in respect of any dividends or other monies thereon or for or on account or in respect of such Member under or in consequence of any such law, together with interest at the rate of fifteen percent (15%) per annum (or such other rate as the Board may determine) thereon from the date of payment to date of repayment, and the Company may deduct or set off against such dividends or other monies so payable any monies paid or payable by the Company as referred to above together with interest at the same rate;

39.3. the Company may recover as a debt due from such Member or his or her executor or administrator (wherever constituted) any monies paid by the Company under or in consequence of any such law and interest thereon at the rate and for the period referred to above in excess of any dividends or other monies then due or payable by the Company; and

39.4. the Company may, if any such money is paid or payable by it under any such law as referred to above, refuse to register a transfer of any Shares by any such Member or his or her executor or administrator until such money and interest is set off or deducted as referred to above or, in the case that it exceeds the amount of any such dividends or other monies then due or payable by the Company, until such excess is paid to the Company.

40. Subject to the rights conferred upon the holders of any class of Shares, nothing in Article 39 will prejudice or affect any right or remedy which any law may confer or purport to confer on the Company. As between the Company and every such Member as referred to above (and, his or her executor, administrator and estate, wherever constituted), any right or remedy which such law shall confer or purport to confer on the Company shall be enforceable by the Company.

CALLS ON SHARES

41. Subject to the terms of allotment, the Board may make calls upon the Members in respect of any monies unpaid on their Shares and each Member (subject to receiving at least fourteen (14) clear days' notice specifying when and where payment is to be made) shall pay to the Company as required by the

notice the amount called on his or her Shares. A call may be required or permitted to be paid in instalments. A call may be revoked before receipt by the Company of a sum due thereunder, in whole or in part, and payment of a call may be postponed in whole or in part.

42. A call shall be deemed to have been made at the time when the resolution of the Board authorising the call was passed.

43. A person on whom a call is made shall (in addition to a transferee) remain liable notwithstanding the subsequent transfer of the Share in respect of which the call is made.

44. The joint holders of a Share shall be jointly and severally liable to pay all calls in respect thereof.

45. If a call remains unpaid after it has become due and payable, the person from whom it is due and payable shall pay interest on the amount unpaid from the day it became due until it is paid at the rate fixed by the terms of allotment of the Share or in the notice of the call or, if no rate is fixed, at the appropriate rate (as defined by the Companies Act), but the Board may waive payment of the interest wholly or in part.

46. An amount payable in respect of a Share on allotment or at any fixed date, whether in respect of nominal value or by way of premium, shall be deemed to be a call and, if it is not paid, the provisions of these Articles shall apply as if that amount had become due and payable by virtue of a call.

47. Subject to the terms of allotment, the Board may make arrangements on the issue of Shares for a difference between the holders in the amounts and times of payment of calls on their Shares.

48. The Directors may, if they think fit, receive from any Member willing to advance the same all or any part of the monies uncalled and unpaid upon any Shares held by him or her, and upon all or any of the monies so advanced may pay (until the same would, but for such advance, become payable) interest at such rate as may be agreed upon between the Directors and the Member paying such sum in advance.

FORFEITURE

49. If a Member fails to pay any call or instalment of a call on the day appointed for payment thereof, the Directors, at any time thereafter during such times as any part of the call or instalment remains unpaid, may serve a notice on him or her requiring payment of so much of the call or instalment as is unpaid together with any interest which may have accrued.

50. The notice shall state a further day (not earlier than the expiration of fourteen (14) clear days from the date of service of the notice) on or before which the payment required by the notice is to be made, and shall state that in the event of non-payment at or before the time appointed, the Shares in respect of which the call was made will be liable to be forfeited.

51. If the requirements of any such notice as aforesaid are not complied with, then at any time thereafter before the payment required by the notice has been made, any Shares in respect of which the notice has been given may be forfeited by a resolution of the Directors to that effect. The forfeiture shall include all dividends or other monies payable in respect of the forfeited Shares and not paid before forfeiture. The Board may accept a surrender of any Share liable to be forfeited hereunder.

52. On the trial or hearing of any action for the recovery of any money due for any call, it shall be sufficient to prove that the name of the Member sued is entered in the Register as the holder, or one of the holders, of the Shares in respect of which such debt accrued, that the resolution making the call is duly recorded in the minute book and that notice of such call was duly given to the Member sued, in pursuance of these Articles, and it shall not be necessary to prove the appointment of the Directors who made such call nor any other matters whatsoever, but the proof of the matters aforesaid shall be conclusive evidence of the debt.

53. A forfeited Share may be sold or otherwise disposed of on such terms and in such manner as the Directors think fit and at any time before a sale or disposition the forfeiture may be cancelled on such terms as the Directors think fit. Where for the purposes of its disposal, such a Share is to be transferred to any person, the Board may authorise some person to execute an instrument of transfer of the Share to that person. The Company may receive the consideration, if any, given for the Share on any sale or disposition thereof and may execute a transfer of the Share in favour of the person to whom the Share is sold or disposed of and thereupon he or she shall be registered as the holder of the Share and shall not be bound to see to the application of the purchase money, if any, nor shall his or her title to the Share be affected by any irregularity or invalidity in the proceedings in reference to the forfeiture, sale or disposal of the Share.

54. A person whose Shares have been forfeited shall cease to be a Member in respect of the forfeited Shares, but nevertheless shall remain liable to pay to the Company all monies which, at the date of forfeiture, were payable by him or her to the Company in respect of the Shares, without any deduction or allowance for the value of the Shares at the time of forfeiture but his or her liability shall cease if and when the Company shall have received payment in full of all such monies in respect of the Shares.

55. A statement in writing that the maker of the statement is a Director or the Secretary of the Company, and that a Share in the Company has been duly forfeited on the date stated in the statement, shall be conclusive evidence of the facts therein stated as against all persons claiming to be entitled to the Share.

56. The provisions of these Articles as to forfeiture shall apply in the case of non-payment of any sum which, by the terms of issue of a Share, becomes payable at a fixed time, whether on account of the nominal value of the Share or by way of premium, as if the same had been payable by virtue of a call duly made and notified.

57. The Directors may accept the surrender of any Share which the Directors have resolved to have been forfeited upon such terms and conditions as may be agreed and, subject to any such terms and conditions, a surrendered Share shall be treated as if it has been forfeited.

NON-RECOGNITION OF TRUSTS

58. The Company shall not be obligated to recognise any person as holding any Share upon any trust (except as is otherwise provided in these Articles or to the extent required by law) and the Company shall not be bound by or be compelled in any way to recognise (even when having notice thereof) any equitable, contingent, future, or partial interest in any Share, or any interest in any fractional part of a Share, or (except only as is otherwise provided by these Articles or the Companies Act) any other rights in respect of any Share except an absolute right to the entirety thereof in the registered holder. This shall not preclude the Company from requiring the Members or a transferee of Shares to furnish the Company with information as to the beneficial ownership of any Share when such information is reasonably required by the Company.

TRANSMISSION OF SHARES

59. If a Member dies, the survivor or survivors where the deceased was a joint holder, and the legal personal representatives of the deceased where he or she was a sole holder or the only survivor of joint holders, shall be the only persons recognised by the Company as having any title to his or her interest in the Shares; but nothing herein contained shall release the estate of any deceased holder from any liability in respect of any Share which had been jointly held by him or her solely or jointly with other persons.

60. A person becoming entitled to a Share in consequence of the death, bankruptcy, liquidation or insolvency of a Member, or otherwise becoming entitled to a Share by operation of any law, directive or regulation (whether of Ireland, the European Union, or any other jurisdiction) may elect, upon such evidence of title being produced as the Directors or the Secretary (or such other person as may be

nominated by the Secretary for this purpose) may reasonably require at any time and from time to time, and subject as further provided in this Article, either to become the holder of the Share or to have some person nominated by him or her registered as the transferee of such Share. If he or she elects to become the holder of the Share, he or she shall give notice to the Company to that effect and, where the Directors or the Secretary (or such other person as may be nominated by the Secretary for this purpose) are satisfied with the evidence of title produced to them, they may register such person as the holder of the Share, subject to the other provisions of these Articles and of the Companies Act. If he or she elects to have another person registered as the transferee of the relevant Share, he or she shall execute an instrument of transfer of the Share to that person. All of these Articles relating to the transfer of Shares shall apply to the notice or instrument of transfer as if it were an instrument of transfer executed by the relevant Member and the event giving rise to the entitlement of the relevant person to the Shares had not occurred.

61. A person becoming entitled to a Share by transmission shall have the rights to which he or she would be entitled if he or she were the holder of the Share (including the right to receive and give a valid discharge for any dividends, distributions or other moneys payable on or in respect of the Share), except that, before being registered as the holder of the Share, he or she shall not be entitled in respect of it to receive notices of, or to attend or vote at, any meeting of the Company or at any separate meeting of holders of any class of Shares in the Company. The Directors or the Secretary (or such other person as may be nominated by the Secretary for this purpose), at any time, may give notice requiring any such person to elect either to be registered himself or herself as the holder of the Share or to transfer the Share and, if the notice is not complied with within ninety (90) days, the Directors or the Secretary (or such other person as may be nominated by the Secretary for this purpose) thereupon may withhold payment of all dividends, bonuses or other monies payable in respect of the Share until the requirements of the notice have been complied with.

AMENDMENT OF MEMORANDUM OF ASSOCIATION; CHANGE OF LOCATION OF REGISTERED OFFICE; AND ALTERATION OF CAPITAL

62. The Company may by Ordinary Resolution (or as otherwise provided in these Articles, or determined by the Board, or otherwise permitted under applicable law):

62.1. divide its share capital into several classes and attach to them respectively any preferential, deferred, qualified or special rights, privileges or conditions;

62.2. increase the authorised share capital by such sum to be divided into Shares of any nominal value;

62.3. consolidate and divide all or any of the Shares into Shares of a larger nominal value than the existing Shares;

62.4. subdivide the Shares, or any of them, into Shares of a smaller nominal value, so however, that in the sub-division the proportion between the amount paid and the amount, if any, unpaid on each reduced Share shall be the same as it was in the case of the Share from which the reduced Share is derived (and so that the Board may determine that, as between the holders of the Shares resulting from such sub-division, one or more of the Shares may have, as compared with the others, any such preferred, deferred or other rights or be subject to any such restrictions as the Company has power to attach to unissued or new Shares);

62.5. cancel any Shares which have not been taken or agreed to be taken by any person and diminish the amount of the Company's share capital by the amount of the Shares so cancelled;

62.6. increase the nominal value of any of the Shares by the addition to them of any undenominated capital;

62.7. reduce the nominal value of any of the Shares by the deduction from them of any part of that value, subject to the crediting of the amount of the deduction to undenominated capital, other than the share premium account;

62.8. convert any undenominated capital into Shares for allotment as bonus shares to holders of existing Shares; and/or

62.9. subject to applicable law, change the currency denomination of its share capital.

63. Subject to the provisions of the Companies Act, the Company may:

63.1. by Special Resolution (or as otherwise required or permitted by applicable law) change its name, alter or add to the Memorandum with respect to any objects, powers or other matters specified therein or alter or add to these Articles;

63.2. by Special Resolution (or as otherwise required or permitted by these Articles and applicable law (including, without limitation, section 83 of the Companies Act)) reduce its issued share capital and any capital redemption reserve fund, share premium account or undenominated capital account. In relation to such reductions, the Company may by Special Resolution (or as otherwise required or permitted by these Articles and applicable law) determine the terms upon which the reduction is to be effected, including in the case of a reduction of part only of any class of Shares, those Shares to be affected; and

63.3. by resolution of the Directors, change the location of its registered office.

64. Where any difficulty arises in regard to any alteration or reorganisation of the share capital of the Company, the Board may settle the same as they think expedient and in particular, may arrange to sell any Shares representing fractions for the best price reasonably obtainable to any person and distribute the proceeds of sale in due proportion among those Members, and the Board may authorise any person to execute an instrument of transfer of the Shares to, or in accordance with the directions of, the purchaser. The transferee shall not be bound to see to the application of the purchase money nor shall his or her title to the Shares be affected by any irregularity in or invalidity of the proceedings in reference to the sale.

CLOSING REGISTER OF MEMBERS OR FIXING RECORD DATE

65. For the purpose of determining Members entitled to notice of or to vote at any meeting of Members or any adjournment thereof, or Members entitled to receive payment of any dividend, or in order to make a determination of Members for any other proper purpose, the Board may provide, subject to the requirements of section 174 of the Companies Act, that the Register of Members shall be closed for transfers at such times and for such periods, not exceeding in the whole thirty (30) days in each year, as it may determine. If the Register of Members shall be so closed for the purpose of determining Members entitled to notice of, or to vote at, a meeting of Members, such Register of Members shall be so closed for at least five (5) days immediately preceding such meeting and the record date for such determination shall be the date of the closure of the Register of Members.

66. In lieu of, or apart from, closing the Register of Members, the Board may fix in advance a date as the record date (a) for any such determination of Members entitled to notice of or to vote at a meeting of the Members, which record date shall not be more than sixty (60) days before the date of such meeting, and (b) 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 sixty (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.

67. If the Register of Members is not so closed and 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 these Articles shall be the record date for such determination of Members. Where a determination of Members entitled to vote at any meeting of Members has been made as provided in these Articles, such determination shall apply to any adjournment thereof; provided, however, that the Directors may fix a new record date of the adjourned meeting, if they think fit.

GENERAL MEETINGS

68. The Board shall convene and the Company shall hold annual general meetings in accordance with the requirements of the Companies Act.

69. The Board may, whenever it thinks fit, and shall, on the requisition in writing of Members holding such number of Shares as is prescribed by, and made in accordance with the Companies Act, convene a general meeting in the manner required by the Companies Act. All general meetings other than annual general meetings shall be called extraordinary general meetings. Where any provision of the Companies Act confers rights on the members of a company to convene a general meeting without first directing the board of directors to convene a general meeting and expresses such rights to apply save where a company's articles of association or constitution provides otherwise, such rights shall not apply to the Members of the Company.

70. The Company shall in each year hold a general meeting as its annual general meeting in addition to any other meeting in that year, and shall specify the meeting as such in the notice calling it. Not more than fifteen (15) months shall elapse between the date of one annual general meeting of the Company and that of the next. Each general meeting shall be held at such time and place as designated by the Board and as specified in the notice of meeting. Subject to section 176 of the Companies Act, all general meetings may be held outside of Ireland.

71. The Board may authorise the Secretary to postpone or cancel any general meeting called in accordance with the provisions of these Articles (other than a meeting requisitioned by the Members in accordance with the Companies Act or the postponement or cancellation of which would be contrary to the Companies Act, law or a Court order pursuant to the Companies Act) if the Board considers that, for any reason, it is impractical or unreasonable to hold the general meeting, provided that notice of postponement or cancellation is given to each Member before the time for such meeting. Fresh notice of the date, time and place for any postponed meeting shall be given to each Member in accordance with the provisions of these Articles.

NOTICE OF GENERAL MEETINGS

72. Subject to the provisions of the Companies Act allowing a general meeting to be called by shorter notice, an annual general meeting, and an extraordinary general meeting called for the passing of a Special Resolution, shall be called on at least twenty-one (21) clear days' notice and all other extraordinary general meetings shall be called on at least fourteen (14) clear days' notice. Such notice shall state the date, time, place of the meeting and the general nature of the business to be considered. Every notice shall specify such other details as are required by applicable law or the relevant code, rules and regulations applicable to the listing of the Shares on any Exchange.

73. A general meeting of the Company shall, whether or not the notice specified in Article 72 has been given and whether or not the provisions of the Articles regarding general meetings have been complied with, be deemed to have been duly convened if applicable law so permits and it is so agreed by the Auditors and by all the Members entitled to attend and vote thereat or by their proxies.

74. The notice convening an annual general meeting shall specify the meeting as such, and the notice convening a meeting to pass a Special Resolution shall specify the intention to propose the resolution as a Special Resolution. Notice of every general meeting shall be given in any manner permitted by these Articles to all Members.

75. There shall appear with reasonable prominence in every notice of general meeting of the Company a statement that a Member entitled to attend and vote is entitled to appoint one or more proxies to attend and vote instead of him or her and that a proxy need not be a Member of the Company.

76. The accidental omission to give notice of a general meeting to, or the non-receipt of notice of a meeting by, any person entitled to receive notice shall not invalidate the proceedings of that meeting.

77. In cases where instruments of proxy are sent out with notices, the accidental omission to send such instrument of proxy to, or the non-receipt of such instrument of proxy by, any person entitled to receive notice shall not invalidate the notice or any resolution passed or any proceeding at any such meeting. A Member present, either in person or by proxy, at any general meeting of the Company or of the holders of any class of Shares in the Company will be deemed to have received notice of that meeting and, where required, of the purpose for which it was called.

PROCEEDINGS AT GENERAL MEETINGS

78. The business of annual general meetings shall include:

78.1. the consideration of the Company's statutory financial statements and the report of the Directors and the report of the Auditors on those statements and that report;

78.2. the review by the Members of the Company's affairs;

78.3. the appointment or re-appointment of Auditors;

78.4. the authorisation of the Directors to approve the remuneration of the Auditors; and

78.5. the election and re-election of Directors.

79. No business shall be transacted at any general meeting unless a quorum is present. One or more Members present in person or by proxy (whether or not such Member actually exercises his voting rights in whole, in part or at all at the relevant general meeting) holding not less than a majority of the issued and outstanding Shares of the Company entitled to vote at the meeting in question shall be a quorum.

80. If within 15 minutes (or such longer time not exceeding one hour as the Chairperson of the meeting may decide to wait) after the time appointed for the holding of the meeting a quorum is not present, or if during the meeting a quorum ceases to be present, the meeting (i) if convened on the requisition of Members, shall be dissolved; and (ii) in any other case, shall stand adjourned to the same day in the next week or to such other day and at such other time and place as the Chairperson (or, in default, the Board) may, subject to the provisions of the Companies Act, determine. If at such adjourned meeting a quorum is not present within 15 minutes after the time appointed for holding it the adjourned meeting shall be dissolved.

81. If the Board wishes to make this facility available to Members for any or all general meetings of the Company, a Member may participate in any general meeting of the Company by means of a telephone, video, electronic or similar communication equipment by way of which all persons participating in such meeting can communicate with each other simultaneously and instantaneously and such participation shall be deemed to constitute presence in person at the meeting.

82. Each Director and the Auditors shall be entitled to attend and speak at any general meeting of the Company.

83. The Chairperson, or in his absence, some other Director nominated by the Directors shall preside at every general meeting of the Company, but if at any meeting neither the Chairperson, nor such other Director, is present within fifteen minutes after the time appointed for the holding of the meeting, or if

none of them are willing to act as Chairperson, the Directors present shall choose some Director present to be Chairperson, or if no Director is present, or if all the Directors present decline to take the chair, the Members present shall choose some Member present to be Chairperson.

84. The Chairperson of the meeting may, and shall if so directed by the meeting (upon the passage of an Ordinary Resolution), adjourn the meeting from time to time and from place to place, but no business shall be transacted at any adjourned meeting other than the business left unfinished, or which might have been transacted, at the meeting from which the adjournment took place. When a general meeting is adjourned for thirty (30) days or more, notice of the adjourned meeting shall be given as in the case of an original meeting; save as aforesaid it shall not be necessary to give any notice of an adjournment or of the business to be transacted at an adjourned general meeting. Without prejudice to any other power of adjournment which the Chairperson of the meeting may have under these Articles, at common law or otherwise, the Chairperson may, without the consent of the meeting, adjourn the meeting from time to time (or indefinitely) and from place to place if he or she decides that it is necessary or appropriate to do so in order to: (a) secure the proper and orderly conduct of the meeting (b) give all persons entitled to do so an opportunity of attending the meeting (c) give all persons entitled to do so a reasonable opportunity of speaking and voting at the meeting or (d) ensure that the business of the meeting is properly concluded or disposed of, including (without limitation) for the purpose of determining the result of a poll.

85.

85.1. Subject to the Companies Act, a resolution may only be put to a vote at a general meeting of the Company or of any class of Members if:

(a) it is specified in the notice of meeting;

(b) it is proposed by or at the direction of the Board;

(c) it is proposed at the direction of a court of competent jurisdiction;

(d) it is proposed pursuant to, and in accordance with, the procedures and requirements of Article 86 or 151;

(e) it is proposed on the requisition in writing of such number of Members as is prescribed by, and is made in accordance with, section 178(3) of the Companies Act;

(f) the Chairperson of the meeting decides that the resolution may properly be regarded as within the scope of the meeting; or

(g) it has not been withdrawn by the Chairperson in accordance with Article 85.2.

85.2. The Chairperson of the meeting may, at his sole discretion, withdraw any resolution to be put to a vote at a general meeting of the Company or of any class of Members and such withdrawal shall not invalidate the proceedings of such meeting and shall be without prejudice to any other resolutions to be put to a vote at such general meeting of the Company or any class of Members.

85.3. No amendment may be made to a resolution, at or before the time when it is put to a vote, unless the Chairperson of the meeting decides that the amendment or the amended resolution may properly be put to a vote at that meeting.

85.4. If the Chairperson of the meeting rules a resolution or an amendment to a resolution admissible or out of order (as the case may be), the proceedings of the meeting or on the resolution in

question shall not be invalidated by any error in his or her ruling. Any ruling by the Chairperson of the meeting in relation to a resolution or an amendment to a resolution shall be final and conclusive.

86.

86.1. For business to be properly requested by a Member to be brought before a general meeting, (other than nominations of directors, which may only be made in accordance with Article 151.1) the Member must:

(a) be a Member of the Company at the time of the giving of the notice for such general meeting;

(b) be entitled to vote at such meeting; and

(c) have given timely and proper notice in writing to the Secretary in accordance with this Article 86.

86.2. To be timely for an annual general meeting, a Member's notice to the Secretary must be delivered to or mailed and received at the registered office of the Company (i) with respect to the first annual general meeting of the Company 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 first made by the Company and (ii) with respect to all other annual general meetings, not less than ninety (90) days nor (except for shareholder proposals subject to Rule14a-8(e)(3) of the Exchange Act) more than one hundred and twenty (120) days prior to the first anniversary of the date of the notice convening the preceding year's annual general meeting provided, however, that if the date of the annual general meeting is changed by more than thirty (30) days from the first anniversary date of the preceding year's annual general meeting, the Member's notice must be so received not earlier than one hundred and twenty (120) days prior to such annual general meeting and not later than the close of business on the later of (x) the 90th day prior to such annual general meeting or (y) the 10th day following the day on which a public announcement of the date of the annual general meeting is first made. In no event shall the adjournment or postponement of any annual general meeting, or the public announcement of such an adjournment or postponement, commence a new time period (or extend any time period) for the giving of a Member's notice to the Secretary pursuant to this Article 86.2.

86.3. To be timely for a general meeting (other than an annual general meeting), a Member's notice to the Secretary must be delivered to or mailed and received at the registered office of the Company not less than ninety (90) days nor (except for shareholder proposals subject to Rule14a-8(e)(3) of the Exchange Act) more than one hundred and twenty (120) days prior to the date of such meeting or, if the first public announcement of the date of such meeting is less than 100 days prior to the date of such meeting, the 10th day following the date on which public announcement is first made of the date of the general meeting. In no event shall the adjournment or postponement of any general meeting, or the public announcement of such an adjournment or postponement, commence a new time period (or extend any time period) for the giving of a Member's notice to the Secretary pursuant to this Article 86.3.

86.4. To be in proper written form, a Member's notice shall set forth as of the date of the notice and as to the Member giving the notice and the beneficial owner, if any, on whose behalf the nomination or proposal is made (each, a Proponent and collectively, the Proponents) as to each matter such Member proposes to bring before the meeting:

(a) a brief description of the business desired to be brought before the meeting and the reasons for conducting such business at the meeting;

(b) the name and address, as they appear in the Register of Members, of each Proponent;

(c) the class, series and number of Shares of the Company which are beneficially owned by each Proponent;

(d) any material interest of the Member, or of any other person on whose behalf such business is raised, in such business;

(e) a description of any agreement, arrangement or understanding (whether oral or in writing) with respect to such nomination or proposal between or among any Proponent and any of its affiliates or associates, and any others (including their names) acting in concert, or otherwise under the agreement, arrangement or understanding, with any of the foregoing;

(f) a representation that the Proponents are holders of record or beneficial owners, as the case may be, of shares of the Company entitled to vote at the meeting and intend to appear in person or by proxy at the meeting to nominate the person or persons specified in the notice (with respect to a notice under Article 151) or to propose the business that is specified in the notice (with respect to a notice under Article 86);

(g) a representation as to whether the Proponents intend to deliver a proxy statement and form of proxy to holders of a sufficient number of holders of the Company's voting shares to elect such nominee or nominees (with respect to a notice under Article 151) or to carry such proposal (with respect to a notice under Article 86);

(h) to the extent known by any Proponent, the name and address of any other Member supporting the proposal on the date of such Member's notice; and

(i) a description of all Derivative Transactions by each Proponent during the previous twelve (12) month period, including the date of the transactions and the class, series and number of securities involved in, and the material economic terms of, such Derivative Transactions.

86.5. The Chairperson shall, if the facts warrant, determine and declare to the meeting that business was not properly brought before the meeting and in accordance with the provisions of this Article and, if he should so determine, he shall so declare to the meeting and any such business not properly brought before the meeting shall not be transacted.

87. Except where a greater majority is required by the Companies Act or where these Articles provide otherwise, any question proposed for a decision of the Members at any general meeting of the Company or a decision of any class of Members at a separate meeting of any class of Shares shall be decided by an Ordinary Resolution.

88. At any general meeting, a resolution put to the vote of the meeting shall be decided on a poll. The Board or the Chairperson may determine the manner in which the poll is to be taken and the manner in which the votes are to be counted.

89. A poll demanded on the election of the Chairperson or on a question of adjournment shall be taken forthwith. A poll demanded on any other question shall be taken at such time as the Chairperson of the meeting directs, and any business other than that on which a poll has been demanded may be proceeded with pending the taking of the poll.

90. No notice need be given of a poll not taken immediately. The result of the poll shall be deemed to be the resolution of the general meeting at which the poll was demanded. On a poll, a Member entitled to

more than one vote need not use all his or her votes or cast all the votes he or she uses in the same way.

91. If authorised by the Board, any vote taken by written ballot may be satisfied by a ballot submitted by electronic and/or telephonic transmission, provided that any such electronic or telephonic submission must either set forth or be submitted with information from which it can be determined that the electronic or telephonic submission has been authorised by the Member or proxy.

92. The Board may adopt such rules, regulations and procedures for the conduct of any meeting of the Members as it deems appropriate. Except to the extent inconsistent with any applicable rules, regulations or procedures adopted by the Board, the Chairperson of any meeting may adopt such rules, regulations and procedures for the meeting, and take such actions with respect to the conduct of the meeting, as the Chairperson of the meeting deems appropriate. The rules, regulations and procedures adopted may include, without limitation, ones that (i) establish an agenda or order of business, (ii) are intended to maintain order and safety at the meeting, (iii) contain limitations on attendance at or participation in the meeting to Members of record of the Company, their duly authorised proxies or such other persons as the Chairperson of the meeting shall determine, (iv) contain restrictions on entry to the meeting after the time fixed for its commencement and (v) limit the time allotted to Member questions or comments.

VOTES OF MEMBERS

93. Subject to any rights or restrictions for the time being attached to any class or classes of Shares, every Member present in person or by proxy shall have one vote for each Share registered in his or her name in the Register of Members.

94. In the case of joint holders of record the vote of the senior holder who tenders a vote, whether in person or by proxy, shall be accepted to the exclusion of the votes of the other joint holders, and for this purpose seniority shall be determined by the order in which the names stand in the Register of Members.

95. A Member of unsound mind, a Member who has made an enduring power of attorney, or in respect of whom an order has been made by any court, having jurisdiction in cases of unsound mind, may vote by his or her committee, donee of an enduring power of attorney, receiver, guardian or other person appointed by the foregoing court, and any such committee, donee of an enduring power of attorney, receiver, guardian or other persons appointed by the foregoing court may vote by proxy.

96. No Member shall be entitled to vote at any general meeting unless he or she is registered as a Member on the record date for such meeting.

97. No objection shall be raised to the qualification of any voter except at the general meeting or adjourned general meeting at which the vote objected to is given or tendered and every vote not disallowed at such general meeting shall be valid for all purposes. Any such objection made in due time shall be referred to the Chairperson of the general meeting whose decision shall be final and conclusive.

98. Unless the Board decides otherwise, no Member shall be entitled to be present or vote at any meeting either personally or by proxy until such Member has paid all calls due and payable on every Share held by him or her whether alone or jointly with any other person together with interest and expenses (if any) to the Company.

99. Section 193 of the Companies Act will not apply to the Company and no resolutions in writing may be validly passed by the members.

PROXIES AND CORPORATE REPRESENTATIVES

100. Votes may be given either personally or by proxy. A Member may appoint more than one proxy or the same proxy under one or more instruments to attend and vote at a meeting and may appoint a proxy to vote both in favour of and against the same resolution in such proportion as specified in the instrument appointing the proxy.

101.

101.1. Every Member entitled to attend and vote at a general meeting may appoint a proxy to attend, speak and vote on his or her behalf and may appoint more than one proxy to attend, speak and vote at the same meeting. The appointment of a proxy or corporate representative shall be in such form and may be accepted by the Company at such place and at such time as may be specified in the notice convening the meeting or in any other information sent to the Members by or on behalf of the Board in relation to the meeting, subject to applicable requirements of the United States Securities and Exchange Commission and any Exchange on which the Shares are listed.

101.2. Without limiting the foregoing, the Board or the Secretary may from time to time permit appointments of a proxy to be made by means of an electronic or internet communication or facility and may in a similar manner permit supplements to, or amendments or revocations of, any such electronic or internet communication or facility to be made. For the avoidance of doubt, such appointments of proxy made by electronic or internet communications (as permitted by the Board or the Secretary) will be deemed to be deposited at the place specified for such purpose once received by the Company. The Board or the Secretary may in addition prescribe the method of determining the time at which any such electronic or internet communication or facility is to be treated as deposited at the place specified for such purpose. The Board may treat any such electronic or internet communication or facility which purports to be or is expressed to be sent on behalf of a Member as sufficient evidence of the authority of the person sending that instruction to send it on behalf of that Member.

102. Any body corporate which is a Member of the Company may authorise such person or persons as it thinks fit to act as its representative at any meeting of the Company or of any class of Members of the Company and the person or persons so authorised shall be entitled to exercise the same powers on behalf of the body corporate which he or she represents as that body corporate could exercise if it were an individual Member of the Company. The Company may require evidence from the body corporate of the due authorisation of such person or persons to act as the representative of the relevant body corporate.

103. An appointment of proxy relating to more than one meeting (including any adjournment thereof) having once been received by the Company for the purposes of any meeting shall not require to be delivered, deposited or received again by the Company for the purposes of any subsequent meeting to which it relates.

104. Receipt by the Company of an appointment of proxy in respect of a meeting shall not preclude a Member from attending and voting at the meeting or at any adjournment thereof which attendance and voting will automatically cancel any proxy previously submitted.

105. An appointment of proxy shall be valid, unless the contrary is stated therein, for any adjournment of the meeting as well as for the meeting to which it relates.

106. A vote given in accordance with the terms of an appointment of proxy or a resolution authorising a representative to act on behalf of a body corporate shall be valid notwithstanding the death or insanity of the principal, or the revocation of the appointment of proxy or of the authority under which the proxy was appointed or of the resolution authorising the representative to act or transfer of the Share in respect of which the proxy was appointed or the authorisation of the representative to act was given, provided that no notice in writing (whether in electronic form or otherwise) of such death, insanity, revocation or transfer shall have been received by the Company at the registered office before the

commencement of the meeting or adjourned meeting at which the appointment of proxy is used or at which the representative acts.

107. The Board may send, at the expense of the Company and subject to applicable law (including the rules and regulations of the United States Securities and Exchange Commission), by post, electronic mail or otherwise, to the Members forms for the appointment of a proxy (with or without stamped envelopes for their return) for use at any general meeting or at any class meeting, either in blank or nominating any one or more of the Directors or any other persons in the alternative.

DIRECTORS

108. The number of Directors on the Board shall be not less than two (2) nor more than 13. The authorised number of Directors (within such fixed maximum and fixed minimum numbers) shall be determined solely by the Board and, for the avoidance of doubt, shall not require approval or ratification by the Company in general meeting.

109. The remuneration to be paid to the Directors shall be such remuneration as the Directors in their sole discretion shall determine. The Directors shall also be entitled to be paid their travelling, hotel and other expenses properly incurred by them in going to, attending and returning from meetings of the Directors, or any committee of the Directors, or general meetings of the Company, or otherwise in connection with the business of the Company, or to receive a fixed allowance in respect thereof as may be determined by the Board from time to time, or a combination partly of one such method and partly the other. The amount, rate or basis of the remuneration or expenses to be paid to the Directors shall not require approval or ratification by the Company in general meeting. A Director is expressly permitted (for the purposes of section 228(1)(d) of the Companies Act) to use the Company's property pursuant to or in connection with: the exercise or performance of his duties, functions and powers as Director or employee; the terms of any contract of service or employment or letter of appointment; and, or in the alternative, any other usage authorised by the Directors (or a person authorised by the Directors) from time to time; and including in each case for a Director's own benefit or for the benefit of another person.

110. The Board may approve additional remuneration to any Director undertaking any special work or services for, or undertaking any special mission on behalf of, the Company other than his or her ordinary routine work as a Director. Any fees paid to a Director who is also counsel or solicitor to the Company, or otherwise serves it in a professional capacity, shall be in addition to his or her remuneration as a Director.

111. The salary or remuneration of a Director appointed to hold employment or executive office may be a fixed sum of money, or wholly or in part governed by business done or profits made, or as otherwise decided by the Board (including, for the avoidance of doubt, by the Board acting through a duly authorised Board committee), and may be in addition to or instead of a fee payable to such Director for his or her services as Director pursuant to these Articles.

112. Members of special or standing committees may be allowed like compensation for service on any such committees or for attending committee meetings, or both.

DIRECTORS' AND OFFICERS' INTERESTS

113. A Director or an officer of the Company who is in any way, whether directly or indirectly, interested in a contract, transaction or arrangement or proposed contract, transaction or arrangement with the Company shall, in accordance with section 231 of the Companies Act, declare the nature of his or her interest at the first opportunity either (a) at a meeting of the Board at which the question of entering into the contract, transaction or arrangement is first taken into consideration, if the Director or officer of the Company 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 (b) by providing a general notice to the Directors declaring that he or she is a Director or an officer of, or has an interest in, a person and is to

be regarded as interested in any transaction or arrangement made with that person, and after giving such general notice it shall not be necessary to give special notice relating to any particular transaction.

114. A Director may hold any other office or place of profit under the Company (other than the office of its Auditors) in conjunction with his or her office of Director for such period and on such terms as to remuneration and otherwise as the Board may determine.

115. Nothing in section 228(1)(e) of the Companies Act shall restrict a Director from entering into any commitment which has been approved by the Board or has been approved pursuant to such authority as may be delegated by the Board in accordance with these Articles. It shall be the duty of each Director to obtain the prior approval of the Board, before entering into any commitment permitted by sections 228(1)(e)(ii) and 228(2) of the Companies Act.

116. A Director may act by himself or herself or by his or her firm in a professional capacity for the Company (other than as its Auditors) and he or she or his or her firm shall be entitled to remuneration for professional services as if he or she were not a Director.

117. A Director may be or become a director, managing director, joint managing director, deputy managing director, executive director, manager or other officer or member of any other entity or otherwise interested in any entity promoted by the Company or in which the Company may be interested as member or otherwise, and no such Director shall be accountable to the Company for any remuneration or other benefits received by him or her as a Director, managing director, joint managing director, deputy managing director, executive director, manager or other officer or member of such other entity; provided that he or she has declared the nature of his or her position with, or interest in, such entity to the Board in accordance with Article 113 and this has been approved by a majority of the disinterested Directors, notwithstanding the fact that the disinterested Directors may represent less than a quorum.

118. No person shall be disqualified from the office of Director or from being an officer of the Company or prevented by such office from contracting with the Company, either as vendor, purchaser or otherwise, nor shall any such contract or any contract or transaction entered into by or on behalf of the Company in which any Director or officer of the Company shall be in any way interested be or be liable to be avoided, nor shall any Director or officer of the Company so contracting or being so interested be liable to account to the Company for any profit realised by any such contract or transaction by reason of such Director or officer of the Company holding office or of the fiduciary relation thereby established; provided that:

    118.1. he or she has declared the nature of his or her interest in such contract or transaction to the Board in accordance with Article 113; and

    118.2. the contract or transaction is approved by a majority of the disinterested Directors, notwithstanding the fact that the disinterested Directors may represent less than a quorum.

119. A Director may be counted in determining the presence of a quorum at a meeting of the Board which authorises or approves the contract, transaction or arrangement in which he or she is interested and he or she shall be at liberty to vote in respect of any contract, transaction or arrangement in which he or she is interested, provided that the nature of the interest of any Director in any such contract or transaction shall be disclosed by him or her in accordance with Article 113, at or prior to its consideration and any vote thereon.

120. For the purposes of Article 113:

    120.1. a general notice given to the Directors that a Director is to be regarded as having an interest of the nature and extent specified in the notice in any transaction or arrangement in which a specified person or class of persons is interested shall be deemed to be a disclosure that the Director has an interest in any such transaction of the nature and extent so specified;

120.2. an interest of which a Director has no knowledge and of which it is unreasonable to expect him or her to have knowledge shall not be treated as an interest of his or hers; and

120.3. a copy of every declaration made and notice given under Article 113 shall be entered within three (3) days after the making or giving thereof in a book kept for this purpose. Such book shall be open for inspection without charge by any Director, Secretary, the Auditors or Member of the Company at the registered office and shall be produced at every general meeting of the Company and at any meeting of the Directors if any Director so requests in sufficient time to enable the book to be available at the meeting.

POWERS AND DUTIES OF DIRECTORS

121. The business of the Company shall be managed by the Directors, who may pay all expenses incurred in promoting and registering the Company and may exercise all such powers of the Company as are not, by the Companies Act or by these Articles, required to be exercised by the Company in general meeting, subject, nevertheless, to any of these Articles and to the provisions of the Companies Act. No resolution made by the Company in general meeting shall invalidate any prior act of the Directors that would have been valid if that resolution had not been made.

122. The Board shall have the power to appoint and remove officers and executives on such terms as the Board sees fit and to give such titles and delegate such responsibilities to those officers and executives as it sees fit.

123. The Company may exercise the powers conferred by section 44 of the Companies Act with regard to having an official seal for use abroad and such powers shall be vested in the Directors.

124. Unless otherwise ordered by the Board, the chief executive officer shall have the authority to exercise the voting powers conferred by shares of any other company held or owned by the Company in such manner in all respects as he or she thinks fit and in particular they may exercise their voting powers in favour of any resolution appointing the directors or any of them as director or officers of such other company or providing for the payment of remuneration or pensions to the directors or officers of such other company. The Board may from time to time confer like powers upon any other person or persons.

125. All cheques, promissory notes, drafts, bills of exchange and other negotiable instruments and all receipts for money paid to the Company shall be signed, drawn, accepted, endorsed or otherwise executed, as the case may be, by such person or persons and in such manner as the Directors shall from time to time by resolution determine.

126. The Directors may from time to time authorise such person or persons as they see fit to perform all acts, including, without prejudice to the foregoing, to effect a transfer of any shares, bonds, or other evidences of indebtedness or obligations, subscription rights, warrants, and other securities in another company in which the Company holds an interest and to issue the necessary powers of attorney for the same; and each such person is authorised on behalf of the Company to vote such securities, to appoint proxies with respect thereto, and to execute consents, waivers and releases with respect thereto, or to cause any such action to be taken.

127. The Board may exercise all powers of the Company to borrow money and to mortgage or charge its 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.

128. The Directors may procure the establishment and maintenance of or participate in, or contribute to, any non-contributory or contributory pension or superannuation fund, scheme or arrangement or life assurance scheme or arrangement for the benefit of, and pay, provide for or procure the grant of donations, gratuities, pensions, allowances, benefits or emoluments to any persons (including Directors or officers) who are or shall have been at any time in the employment or service of the Company or of

any company which is or was a subsidiary or holding company of the Company or of any predecessor in business of the Company or any such subsidiary or holding company and the wives, husbands, widows, widowers, families, relatives or dependants of any such persons. The Directors may also procure the establishment and subsidy of or subscription to and support of any institutions, associations, clubs, funds or trusts calculated to be for the benefit of any such persons as aforesaid or otherwise to advance the interests and well-being of the Company or of any such other company as aforesaid or its Members, and payments for or towards the issuance of any such persons as aforesaid and subscriptions or guarantees of money for charitable or benevolent objects or for any exhibition or for any public, general or useful object; provided that any Director shall be entitled to retain any benefit received by him or her under this Article 128, subject only, where the Companies Act requires, to disclosure to the Members and the approval of the Company in general meeting.

129. The Board may from time to time provide for the management of the affairs of the Company in such manner as it shall think fit and the specific delegation provisions contained in the Articles shall not limit the general powers conferred by these Articles.

MINUTES

130. The Board shall cause minutes to be made in books kept for the purpose of all (i) appointments of officers and committees made by the Board (ii) resolutions and proceedings at meetings of (a) the Company or of the holders of any class of Shares and (b) the Board and of committees of the Board, including in each case the names of the Directors and others present at each meeting. Any such minutes, if signed by the Chairperson of the meeting at which the proceedings were held or by the Chairperson of the next succeeding meeting or the Secretary, shall be prima facie evidence of the matters stated in them.

DELEGATION OF THE BOARD'S POWERS

131. The Board may delegate any of its powers (with power to sub-delegate) to any committee consisting of one or more Directors and/or (if thought fit) one or more other persons. The Board may also delegate to any Director, officer or member of the management of the Company or any of its subsidiaries such of its powers as it considers desirable to be exercised by him or her. The Board may also designate one or more persons as alternate members of any committee, who may replace any absent or disqualified member at any meeting of any such committee. Any such delegation may be made subject to any conditions the Board may impose, and either collaterally with or to the exclusion of its own powers, and may be revoked or altered. Subject to any such conditions, the proceedings of a committee shall be governed by the Articles regulating the proceedings of Directors, so far as they are capable of applying. Each committee shall keep regular minutes and report to the Board when required. Unless otherwise determined by the Board, the quorum necessary for the transaction of any business at any committee meeting shall be a majority of the members of such committee. Where a provision of the Articles refers to the exercise of a power, authority or discretion by the Board and that power, authority or discretion has been delegated by the Board to a committee, the provision shall be construed as permitting the exercise of the power, authority or discretion by the committee.

132. The Board may, by power of attorney or otherwise, appoint any person to be the agent of the Company on such conditions as the Board may determine, provided that the delegation is not to the exclusion of its own powers and may be revoked by the Board at any time.

133. The Board may, by power of attorney or otherwise, appoint any company, firm, person or body of persons, whether nominated directly or indirectly by the Board, to be the attorney or authorised signatory of the Company for such purpose and with such powers, authorities and discretions (not exceeding those vested in or exercisable by the Board under these Articles) and for such period and subject to such conditions as they may think fit, and any such powers of attorney or other appointment may contain such provisions for the protection and convenience of persons dealing with any such attorneys or authorised signatories as the Board may think fit and may also authorise any such attorney

or authorised signatory to delegate all or any of the powers, authorities and discretions vested in him or her.

CHAIRPERSON AND EXECUTIVE OFFICERS

134. The Board may elect any Director as Chairperson of the Board and determine the period for which he or she is to hold office.

135. In addition to the Chairperson, the Directors and the Secretary, the Company may appoint such other officers, including executive officers, as the Board may from time to time determine and, without limitation to the foregoing, the Board may appoint any person (whether or not a Director) to fill the following positions: chief executive officer, chief financial officer, general counsel, president, treasurer and controller. Any person may hold more than one of the foregoing positions.

136. Any person elected or appointed pursuant to Articles 134 and 135 shall hold his or her office or other position for such period and on such terms as the Board may determine and the Board may revoke or vary any such election or appointment at any time by resolution of the Board. Any such revocation or variation shall be without prejudice to any claim for damages that such person may have against the Company or the Company may have against such person for any breach of any contract of service between him or her and the Company which may be involved in such revocation or variation. If any such office or other position becomes vacant for any reason, the vacancy may be filled by the Board.

137. Except as provided in the Companies Act or these Articles, the powers and duties of any person elected or appointed to any office or executive or official position pursuant to Articles 134 and 135 shall be such as are determined from time to time by the Board.

138. Any officer may resign at any time by giving written notice to the Company. The resignation is effective without acceptance when the notice is given to the Company, unless a later effective date is specified in the notice.

139. The use of the word “officer”, “director” (save where the relevant person is a Director for the purposes of these Articles) (or similar words) in the title of any executive or other position shall not be deemed to imply that the person holding such executive or other position is an “officer” or “director” of the Company within the meaning of the Companies Act.

PROCEEDINGS OF DIRECTORS

140. Except as otherwise provided by these Articles, the Directors shall meet together for the despatch of business, convening, adjourning and otherwise regulating their meetings and procedures as they think fit. Questions arising at any meeting shall be decided by a majority of votes of the Directors present at a meeting at which there is a quorum. Each Director shall have one vote.

141. Regular meetings of the Board may be held at such times and places as may be provided for in resolutions adopted by the Board. No additional notice of a regularly scheduled meeting of the Board shall be required.

142. A Director may, and the Secretary on the requisition of a Director shall, at any time summon a meeting of the Directors by at least 24 hours’ notice (or, if notice is mailed, at least four calendar days’ notice) in writing to every Director, unless notice is waived by all the Directors either at, before or after the meeting is held and, provided further, if notice is given in person, by telephone, cable, telex, telecopy or email, the same shall be deemed to have been given on the day it is delivered to the Directors or transmitting organisation, as the case may be. The accidental omission to give notice of a meeting of the Directors to, or the non-receipt of notice of a meeting by, any person entitled to receive notice shall not invalidate the proceedings of that meeting. The presence of a Director at a meeting of the Directors shall be deemed to be a waiver of any failure to give due notice of such meeting unless such Director states that he or she is not waiving any such failure promptly following the calling to order of such

meeting. Notice of a Board meeting shall be deemed to be duly given to a Director if it is given to such Director personally or by word of mouth or sent in writing to his or her last known address or any other address given to the Company by such Director for such purpose or given by electronic communications to an address for the time being notified to the Company by the Director. In this Article "address," in relation to documents in electronic form, includes any number or address used for the supply of documents in electronic form.

143. The quorum necessary for the transaction of the business of the Board shall be a majority of the Directors in office. If a quorum shall not be present at any meeting of the Board, the Directors present thereat may adjourn the meeting from time to time, without notice other than announcement at the meeting, until a quorum shall be present.

144. The continuing Directors may act notwithstanding any vacancy in their body, but if and so long as their number is reduced below the number fixed by or pursuant to these Articles as the minimum number of Directors, the continuing Directors or Director may act for the purpose of increasing the number of Directors to that number, or of summoning a general meeting of the Company, but for no other purpose. If there are no Director or Directors able or willing to act, any two Members may summon a general meeting for the purpose of appointing Directors. Any Director so appointed shall hold office (subject to these Articles) only until the dissolution of the annual general meeting next following such appointment unless such Director is re-elected during such meeting.

145. If no Chairperson is elected, or if at any meeting the Chairperson is not present within five (5) minutes after the time appointed for holding the same, the Directors present may choose one of their number to be the Chairperson of the meeting or proceed without a Chairperson of the meeting.

146. All acts done by any meeting of the Directors or of a committee of Directors shall, notwithstanding that it be afterwards discovered that there was some defect in the appointment of any Director, or that they or any of them were disqualified, be as valid as if every such person had been duly appointed and qualified to be a Director.

147. Members of the Board or of any committee thereof may participate in a meeting of the Board or of such committee by means of conference telephone or similar communications equipment by means of which all persons participating in the meeting can hear each other and participation in a meeting pursuant to this provision shall constitute presence in person at such meeting. Unless otherwise determined by the Directors, the meeting shall be deemed to be held at the place where the telephone call or similar communication was initiated.

148. A resolution or other document in writing (in electronic form or otherwise), signed (whether by electronic signature, advanced electronic signature or otherwise as approved by the Directors) by all the Directors entitled to receive notice of a meeting of Directors or of a committee of Directors, and to vote on the relevant resolution or matter, shall be as valid and effectual as if it had been passed at a meeting of Directors or (as the case may be) a committee of Directors duly convened and held and may consist of several documents in the like form each signed by one or more Directors, and such resolution or other document or documents when duly signed may be delivered or transmitted (unless the Directors shall otherwise determine either generally or in any specific case) by facsimile transmission, electronic mail or some other similar means of transmitting the content of documents.

RESIGNATION AND DISQUALIFICATION OF DIRECTORS

149. The office of a Director shall be vacated ipso facto:

149.1. on the death of a Director;

149.2. if he or she resigns his or her office, on the date on which notice of his or her resignation is delivered to the registered office or tendered at a meeting of the Board or on such later date as may be specified in such notice;

149.3. if he or she ceases to be a Director by virtue of any provision of the Companies Act, is removed from office pursuant to these Articles or the Companies Act or becomes prohibited by law from being a Director;

149.4. if he or she becomes bankrupt, has an interim receiving order made against him or her, makes any arrangement or compounds with his or her creditors generally or applies to the court for an interim order in connection with a voluntary arrangement under any legislation relating to insolvency;

149.5. if the health of the director is such that, in the opinion of a majority of the other Directors, he or she can no longer be reasonably regarded as possessing adequate decision making capacity;

149.6. in the case of a Director who holds executive office, his or her appointment to such office is terminated or expires and the Board resolves that such Director's office be vacated;

149.7. if he or she is absent, without permission of the Board, from Board meetings for six consecutive months and the Board resolves that his or her office be vacated; or

149.8. if the Director is requested to resign in writing by not less than a majority of the other Directors.

150. A resolution of the Board declaring a Director to have vacated office pursuant to this Article shall be conclusive as to the fact and grounds of vacation stated in the resolution.

APPOINTMENT, ROTATION AND NOMINATION OF DIRECTORS

151.

151.1. No person shall be appointed a Director unless nominated in accordance with the provisions of this Article 151. Nominations of persons for election to the Board at a general meeting may be made:

(a) by or at the direction of the Board or a committee thereof;

(b) with respect to election at a general meeting, by any Member who holds Shares carrying the general right to vote at general meetings of the Company, who is a Member at the time of the giving of the required notice of the relevant general meeting provided for in these Articles and at the time of the relevant general meeting, and who has given timely and proper notice in writing to the Secretary in accordance with Article 151.2 and 151.3;

(c) with respect to election at an extraordinary general meeting requisitioned in accordance with section 178(3) of the Companies Act, by a Member or Members who hold Shares carrying the general right to vote at general meetings of the Company and who make such nomination in the written requisition of the extraordinary general meeting in accordance with these Articles, including Article 151.3, and the provisions of the Companies Act relating to nominations of Directors and the proper bringing of special business before an extraordinary general meeting,

(sub-clauses (b) and (c) being the exclusive means for a Member to make nominations of persons for election to the Board).

151.2. For nominations of persons for election as Directors at a general meeting to be timely, a Member's notice must comply with the requirements of Article 86.2 or 86.3 (as applicable).

151.3. To be in proper written form, a Member's notice for nomination(s) of person(s) for election pursuant to Article 151.1(b), or in the case of nomination(s) of person(s) for election pursuant to

Article 151.1(c), a Member's written requisition of the extraordinary general meeting, must, in addition to any other applicable requirements, set forth:

(a) as to each person whom the Member proposes to nominate for election or re-election as a Director, all information relating to such person that is required to be disclosed in solicitations for proxies for election of directors, or is otherwise required, in each case pursuant to Section 14 of the Exchange Act and the rules and regulations promulgated thereunder (including such person's written consent to being named in the proxy statement as a nominee and to serving as a director if elected); and

(b) as to the Member giving the notice and each Proponent, the information required in Article 86.4.

151.4. The Chairperson of the meeting shall determine whether a nomination was made in accordance with the procedures prescribed by these Articles, and if he or she should determine that such nomination was not made in accordance with such procedures, he or she shall declare to the meeting that the nomination was defective and such defective nomination shall be disregarded. Any such ruling by the Chairperson of the meeting shall be final and conclusive.

151.5. The Company may require any proposed nominee to furnish such other information as it may reasonably require, including the completion of any questionnaires, to determine the eligibility of such proposed nominee to serve as a Director of the Company and the impact that such service would have on the ability of the Company to satisfy the requirements of laws, rules, regulations and listing standards applicable to the Company or its Directors.

152. The Directors shall be divided into three classes, designated Class I, Class II and Class III. The initial division of the Board into classes shall be made by the decision of the affirmative vote of a majority of the Directors in office and each class need not be of equal size or number.

152.1. The term of the initial Class I directors shall terminate at the conclusion of the Company's 2019 annual general meeting; the term of the initial Class II directors shall terminate on the conclusion of the Company's 2020 annual general meeting; and the term of the initial Class III directors shall terminate on the conclusion of the Company's 2021 annual general meeting.

152.2. At each of the subsequent annual general meetings of the Company beginning with the Company's 2019 annual general meeting, all of the Directors of the class of directors whose term expires on the conclusion of that annual general meeting shall retire from office, unless re-elected, and successors to that class of directors shall be elected for a three-year term.

152.3. The resolution appointing any Director must designate the Director as a Class I, Class II or Class III Director.

152.4. Every Director of the class retiring shall be eligible to stand for re-election at an annual general meeting.

152.5. If the number of Directors is changed, any increase or decrease shall be apportioned among the classes so as to maintain the number of Directors in each class as nearly equal as possible or as the Chairman may otherwise direct. In no case will a decrease in the number of Directors shorten the term of any incumbent Director.

152.6. A Director shall hold office until the conclusion of the annual general meeting for the year in which his term expires, subject however, to prior death, resignation, retirement, disqualification or removal from office.

152.7. Notwithstanding any other provision of these Articles, the Directors may appoint a person who is willing to act to be a Director, either to fill a casual vacancy or as an additional Director, provided that the appointment does not cause the number of Directors to exceed the number prescribed by the Board in accordance with Article 108. A casual vacancy will include, without limitation, a vacancy that results from the death, resignation, retirement, disqualification or removal of a Director.

152.8. Any Director of such class elected to fill a vacancy resulting from an increase in the number of Directors of such class shall hold office for a term that shall coincide with the remaining term of that class. Any Director elected to fill a vacancy not resulting from an increase in the number of Directors shall have the same remaining term as that of his predecessor.

153. Directors will be elected by way of Ordinary Resolution of the Company in general meeting, provided that if the number of Director nominees exceeds the number of Directors (as determined by the Board) to be elected at such meeting (a "contested election"), each of those nominees shall be voted upon as a separate resolution and the Directors shall be elected by a plurality of the votes of the Shares present in person or represented by proxy at any such meeting and entitled to vote on the election of Directors. For the purposes of this Article 153, "elected by a plurality" means the election of those Director nominees, equal in number to the number of positions to be filled at the relevant general meeting (as determined by the Board), that received the highest number of votes in the contested election. Cumulative voting is prohibited in the election of Directors.

REMOVAL OF DIRECTORS

154. The Company may, by Ordinary Resolution, of which notice has been given in accordance with section 146 of the Companies Act, remove any Director before the expiration of his or her period of office notwithstanding anything in these Articles or in any agreement between the Company and such Director. Such removal shall be without prejudice to any claim such Director may have for damages for breach of any contract of service between him or her and the Company.

SECRETARY

155. The Board shall appoint the Secretary and may appoint one or more persons to be a joint, deputy or Assistant Secretary at such remuneration (if any) and on such terms as the Board sees fit and any person so appointed may be removed by the Board at any time.

156. The duties of the Secretary shall be those prescribed by the Companies Act, together with such other duties as shall from time to time be prescribed by the Board, and in any case, shall include the making and keeping of records of the votes, doings and proceedings of all meetings of the Members and the Board of the Company, and committees, and the authentication of records of the Company.

157. A provision of the Companies Act or these Articles requiring or authorising a thing to be done by or to a Director and the Secretary shall not be satisfied by its being done by or to the same person acting both as Director and as, or in the place of, the Secretary.

SEAL

158. Company may, if the Board so determines, have a Seal (including any official seals kept pursuant to the Companies Act) which shall only be used by the authority of the Board or of a committee of the Board authorised by the Board in that regard and every instrument to which the Seal has been affixed shall be signed by any person who shall be either a Director or the Secretary or some other person authorised by the Board, either generally or specifically, for the purpose.

159. The Company may have for use in any place or places outside Ireland a duplicate Seal or Seals, each of which shall be a duplicate of the Seal of the Company, except, in the case of a seal for use in sealing documents creating or evidencing securities issued by the Company, for the addition on its face of the

word “Securities” and, if the Board so determines, with the addition on its face of the name of every place where it is to be used.

DIVIDENDS, DISTRIBUTIONS AND RESERVES

160. The Company in general meeting may by Ordinary Resolution declare dividends, but no dividends shall exceed the amount recommended by the Board. Subject to the Companies Act, the Board may, from time to time, pay such interim dividends as appear to it to be justified by the profits of the Company available for distribution. The Board may direct that any dividend declared by the Company in general meeting or by the Board in accordance with these Articles, may be paid wholly or partly by the distribution of specific assets and in particular of paid up shares, debentures or debenture stocks of any other company or in any one or more of such ways. Where any difficulty arises in regard to such distribution, the Board may settle the same as they think expedient, and in particular may issue fractional certificates or ignore fractions, fix the value for distribution of such specific assets or any part thereof and may determine that cash payments shall be made to any Members upon the footing of the value so fixed, in order to adjust the rights of all the parties, and may vest any such specific assets in trustees as may seem expedient to the Board.

161. Subject to the Companies Act, the Board may from time to time declare dividends (including interim dividends) and distributions on Shares outstanding and authorise payment of the same out of the funds of the Company lawfully available therefore and in any currency chosen at its discretion.

162. The Board may, before recommending or declaring any dividends or distributions, set aside such sums as it thinks proper as a reserve or reserves which shall, as directed by the Board, be applicable for any purpose of the Company and pending such application may, as directed by the Board, be employed in the business of the Company or be invested in such investments as the Directors may lawfully determine. The Directors may also, without placing the same to reserve, carry forward any profits which they may think it prudent not to dividend or distribute.

163. No dividend, interim dividend or distribution shall be paid otherwise than in accordance with the provisions of section 117 of the Companies Act.

164. Subject to the rights of persons, if any, entitled to Shares with special rights as to dividends or distributions, if dividends or distributions are to be declared on a class of Shares, they shall be declared and paid according to the amounts paid or credited as paid on the Shares of such class outstanding on the record date for such dividend or distribution as determined in accordance with these Articles.

165. The Directors may deduct from any dividend payable to any Member all sums of money (if any) immediately payable by him or her to the Company in relation to his or her Shares.

166. Any dividend, distribution, interest or other monies payable in cash in respect of Shares may be paid by cheque or warrant sent through the post, or sent by any electronic or other means of payment, directed to the registered address of the holder or, in the case of joint holders, to the holder who is first named on the Register of Members or to such person and to such address as such holder or joint holders may in writing direct. Every such cheque or warrant, electronic or other payment shall be made payable to the order of the person to whom it is sent and payment of the cheque or warrant shall be a good discharge to the Company. Any one of two or more joint holders may give effectual receipts for any dividends, bonuses, or other monies payable in respect of the Share held by them as joint holders. Any such dividend or other distribution may also be paid by any other method (including payment in a currency other than US$, electronic funds transfer, direct debit, bank transfer or by means of a relevant system) which the Directors consider appropriate and any Member who elects for such method of payment shall be deemed to have accepted all of the risks inherent therein. The debiting of the Company’s account in respect of the relevant amount shall be evidence of good discharge of the Company’s obligations in respect of any payment made by any such methods.

167. No dividend or distribution shall bear interest against the Company.

168. All unclaimed dividends or other monies payable by the Company in respect of a Share may be invested or otherwise made use of by the Board for the benefit of the Company until claimed. If the Directors so resolve, subject to applicable law, any dividend which has remained unclaimed for twelve (12) years from the date of its declaration shall be forfeited and cease to remain owing by the Company. The payment by the Directors of any unclaimed dividend or other monies payable in respect of a Share into a separate account shall not constitute the Company a trustee in respect thereof.

169. If, in respect of a dividend or other amount payable in respect of a Share (i) a cheque, warrant or money order is returned undelivered or left uncashed or (ii) a transfer made by or through a bank transfer system and/or other funds transfer system(s) fails or is not accepted, on two consecutive occasions, or one occasion and reasonable enquiries have failed to establish another address or account of the person entitled to the payment, the Company shall not be obliged to send or transfer a dividend or other amount payable in respect of such Share to such person until he or she notifies the Company of an address or account to be used for such purpose.

CAPITALISATION

170. Without prejudice to any powers conferred on the Directors as aforesaid, and subject to the Board's authority to issue and allot Shares under Article 7, the Board may:

170.1. resolve to capitalise an amount standing to the credit of reserves (including, without limitation, a share premium account, undenominated capital account, capital redemption reserve and profit and loss account), whether or not available for distribution;

170.2. appropriate the sum resolved to be capitalised to the Members in proportion to the nominal amount of Shares held by them respectively and apply that sum on their behalf in or towards paying up in full unissued Shares or debentures of a nominal amount equal to that sum, and allot the Shares or debentures, credited as fully paid, to the Members (or as the Board may direct) in those proportions, or partly in one way and partly in the other, but the share premium account, undenominated capital account, capital redemption reserve and profits that are not available for distribution may, for the purposes of this Article 170, only be applied in paying up unissued Shares to be allotted to Members credited as fully paid;

170.3. make any arrangements it thinks fit to resolve a difficulty arising in the distribution of a capitalised reserve, including that where Shares or debentures become distributable in fractions, the Board may deal with the fractions as it thinks fit;

170.4. authorise a person to enter (on behalf of all the Members concerned) into an agreement with the Company providing for the allotment to the Members respectively, credited as fully paid, of Shares or debentures to which they may be entitled on the capitalisation and any such agreement made under this authority being effective and binding on all those Members; and

170.5. generally do all acts and things required to give effect to the resolution of the Board.

171. Any such capitalisation will not require approval or ratification by the Members of the Company.

ACCOUNTS

172. The Board shall, in accordance with Chapter 2 of Part 6 of the Companies Act, cause to be kept adequate accounting records, whether in the form of documents, electronic form or otherwise, that:

172.1. correctly record and explain the transactions of the Company;

172.2. will at any time enable the financial position of the Company to be determined with reasonable accuracy;

172.3. will enable the Board to ensure that any financial statements of the Company comply with the requirements of the Companies Act;

172.4. will record all sums of money received and expended by the Company and the matters in respect of which the receipt or expenditure takes place, all sales and purchases of goods by the Company and the assets and liabilities of the Company; and

172.5. will enable the financial statements of the Company to be readily and properly audited.

173. Accounting records shall be kept on a continuous and consistent basis and entries therein shall be made in a timely manner and be consistent from year to year. The Company may send by post, electronic mail or any other means of electronic communication a summary financial statement to its Members or persons nominated by any Member. The Company may meet, but shall be under no obligation to meet, any request from any of its Members to be sent additional copies of its full report and accounts or summary financial statement or other communications with its Members.

174. The accounting records shall be kept at the registered office of the Company or, subject to the provisions of the Companies Act, at such other place as the Directors think fit and shall be open at all reasonable times to the inspection of the Directors.

175. Accounting records shall not be deemed to be kept as required by Articles 172 to 174 if there are not kept such accounting records as are necessary to give a true and fair view of the state of the Company's affairs and to explain its transactions.

176. In accordance with the provisions of the Companies Act, the Board may from time to time cause to be prepared and to be laid before the Company in general meeting profit and loss accounts, balance sheets, group accounts (if any) and such other reports and accounts as may be required by law.

177. A copy of every balance sheet (including every document required by law to be annexed thereto) which is to be laid before the annual general meeting of the Company together with a copy of the Directors' report and Auditors' report shall be sent by post, electronic mail or any other means of communication (electronic or otherwise), not less than twenty-one (21) clear days before the date of the annual general meeting, to every person entitled under the provisions of the Companies Act to receive them; provided that in the case of those documents sent by electronic mail or any other means of electronic communication, such documents shall be sent with the consent of the recipient, to the address of the recipient notified to the Company by the recipient for such purposes.

AUDIT

178. Auditors shall be appointed and their duties regulated in accordance with Part 6, Chapter 18 of the Companies Act or any statutory amendment thereof, any other applicable law and such requirements not inconsistent with the Companies Act as the Board may from time to time determine.

NOTICES

179. Any notice to be given, served, sent or delivered pursuant to these Articles shall be in writing (whether in electronic form or otherwise).

179.1. A notice or document to be given, served, sent or delivered in pursuance of these Articles, and the annual report of the Company, may be given to, served on or delivered to any Director, Member or committee member by the Company:

(a) by handing same to their authorised agent;

(b) by delivering same to their registered address;

(c) by sending same by the post in a pre-paid cover addressed to their registered address; or

(d) by sending, with the consent of the Director, Member or committee member to the extent required by law, same by means of electronic mail or other means of electronic communication approved by the Directors or the Secretary (or such other person as may be nominated by the Secretary for this purpose), to the address of the Director, Member or committee member notified to the Company by the Director, Member or committee member for such purpose (or if not so notified, then to the address of the Director, Member or committee member last known to the Company). A notice or document may be sent by electronic means to the fullest extent permitted by the Companies Act.

179.2. For the purposes of these Articles and the Companies Act, a document, including the Company's financial statements and the directors' and auditor's reports thereon, shall be deemed to have been sent to a Director, Member or committee member if a notice is given, served, sent or delivered to the Director, Member or committee member and the notice specifies the website or hotlink or other electronic link at or through which the Director, Member or committee member may obtain a copy of the relevant document.

179.3. Where a notice or document is given, served or delivered pursuant to sub-paragraph 179.1(a) or 179.1(b) of this Article, the giving, service or delivery thereof shall be deemed to have been effected at the time the same was handed to the Director, Member or committee member or his or her authorised agent, or left at his or her registered address (as the case may be).

179.4. Where a notice or document is given, served or delivered pursuant to sub-paragraph 179.1(c) of this Article, the giving, service or delivery thereof shall be deemed to have been effected at the expiration of twenty-four (24) hours after the cover containing it was posted. In proving service or delivery it shall be sufficient to prove that such cover was properly addressed, stamped and posted.

179.5. Where a notice or document is given, served or delivered pursuant to sub-paragraph 179.1(d) of this Article, the giving, service or delivery thereof shall be deemed to have been effected at the expiration of forty-eight (48) hours after despatch.

179.6. Every legal personal representative, committee, receiver, curator bonis or other legal curator, assignee in bankruptcy, examiner or liquidator of a Member shall be bound by a notice given as aforesaid if sent to the last registered address of such Member, or, in the event of notice given or delivered pursuant to sub-paragraph 179.1 (d), if sent to the address notified to the Company by the Member for such purpose notwithstanding that the Company may have notice of the death, lunacy, bankruptcy, liquidation or disability of such Member.

179.7. Notwithstanding anything contained in this Article to the contrary, the Company shall not be obliged to take account of or make any investigations as to the existence of any suspension or curtailment of postal services within or in relation to all or any part of any jurisdiction.

179.8. Any requirement in these Articles for the consent of a Member in regard to the receipt by such Member of electronic mail or other means of electronic communications approved by the Directors, including the receipt of the Company's annual report, statutory financial statements and the Directors' and auditor's reports thereon, shall be deemed to have been satisfied where the Company has written to the Member informing him or her of its intention to use electronic communications for such purposes and the Member has not, within four (4) weeks of the issue of such notice, served an objection in writing on the Company to such proposal. Where a Member has given, or is deemed to have given, his/her consent to the receipt by such Member of electronic mail or other means of electronic communications approved by the Directors, she/he may revoke such consent at any time by requesting the Company to communicate with

him or her in documented form; provided, however, that such revocation shall not take effect until five (5) days after written notice of the revocation is received by the Company. No such consent shall be necessary, and to the extent it is necessary, such consent shall be deemed to have been given, if electronic communications are permitted to be used under the rules and regulations of the United States Securities and Exchange Commission or any Exchange on which the Shares or other securities of the Company are listed.

179.9. Without prejudice to the provisions of sub-paragraphs 179.1 (a) and 179.1(b) of this Article, if at any time by reason of the suspension or curtailment of postal services in any territory, the Company is unable effectively to convene a general meeting by notices sent through the post, a general meeting may be convened by a public announcement (as defined below) and such notice shall be deemed to have been duly served on all Members entitled thereto at noon (New York time) on the day on which the said public announcement is made. In any such case the Company shall put a full copy of the notice of the general meeting on its website. A "public announcement" shall mean disclosure in a press release reported by a financial news service or in a document publicly filed by the Company with the United States Securities and Exchange Commission pursuant to sections 13, 14 or 15(d) of the Exchange Act and the rules and regulations promulgated thereunder.

180. Notice may be given by the Company to the joint holders of a Share by giving the notice to the joint holder whose name stands first in the Register in respect of the Share and notice so given shall be sufficient notice to all the joint holders.

181.

181.1. Every person who becomes entitled to a Share shall, before his or her name is entered in the Register in respect of the Share, be bound by any notice in respect of that Share which has been duly given to a person from whom he or she derives his or her title.

181.2. A notice may be given by the Company to the persons entitled to a Share in consequence of the death or bankruptcy of a Member by sending or delivering it, in any manner authorised by these Articles for the giving of notice to a Member, addressed to them at the address, if any, supplied by them for that purpose. Until such an address has been supplied, a notice may be given in any manner in which it might have been given if the death or bankruptcy had not occurred.

182. The signature (whether electronic signature, an advanced electronic signature or otherwise) to any notice to be given by the Company may be written (in electronic form or otherwise) or printed.

183. A Member present, either in person or by proxy, at any meeting of the Company or the holders of any class of Shares in the Company shall be deemed to have received notice of the meeting and, where requisite, of the purposes for which it was called.

UNTRACED HOLDERS

184.

184.1. Subject to applicable law, the Company shall be entitled to sell, at the best price reasonably obtainable, any Share or stock of a Member or any Share or stock to which a person is entitled by transmission if and provided that:

(a) for a period of twelve (12) years (not less than three (3) dividends having been declared and paid) no cheque or warrant sent by the Company through the post in a prepaid letter addressed to the Member or to the person entitled by transmission to the Share or stock at his or her address on the Register or other than the last known address given by the Member or the person entitled by transmission to which cheques and warrants

are to be sent has been cashed and no communication has been received by the Company from the Member or the person entitled by transmission; and

(b) at the expiration of the said period of twelve (12) years, the Company has given notice by advertisement in a leading newspaper circulating in the area in which the address referred to in paragraph (a) of this Article is located of its intention to sell such Share or stock; and

(c) the Company has not during the further period of three (3) months after the date of the advertisement and prior to the exercise of the power of sale received any communication from the Member or person entitled by transmission.

184.2. To give effect to any such sale, the Company may appoint any person to execute as transferor an instrument of transfer of such Share or stock and such instrument of transfer shall be as effective as if it had been executed by the Member or person entitled by transmission to such Share or stock. The Company shall account to the Member or other person entitled to such Share or stock for the net proceeds of such sale by carrying all monies in respect thereof to a separate account which shall be a permanent debt of the Company and the Company shall be deemed to be a debtor and not a trustee in respect thereof for such Member or other person. Monies carried to such separate account may either be employed in the business of the Company or invested in such investments (other than shares of the Company or its holding company if any) as the Directors may from time to time think fit.

184.3. To the extent necessary in order to comply with any laws or regulations to which the Company is subject in relation to escheatment, abandonment of property or other similar or analogous laws or regulations ("**Applicable Escheatment Laws**"), the Company may deal with any Share of any Member and any unclaimed cash payments relating to such Share in any manner which it sees fit, including transferring or selling such Share and transferring to third parties any unclaimed cash payments relating to such Share.

184.4. The Company may only exercise the powers granted to it in paragraph 184.1 above in circumstances where it has complied with, or procured compliance with, the required procedures (as set out in the Applicable Escheatment Laws) with respect to attempting to identify and locate the relevant member of the Company.

184.5. Any stock transfer form to be executed by the Company in order to sell or transfer a Share pursuant to Article 184.1 may be executed in accordance with Article 24.1.

DESTRUCTION OF DOCUMENTS

185. Subject to applicable law, the Company may destroy:

185.1. any dividend mandate or any variation or cancellation thereof or any notification of change of name or address, at any time after the expiry of two (2) years from the date such mandate variation, cancellation or notification was recorded by the Company;

185.2. any instrument of transfer of Shares which has been registered, at any time after the expiry of six (6) years from the date of registration; and

185.3. any other document on the basis of which any entry in the Register was made, at any time after the expiry of six (6) years from the date an entry in the Register was first made in respect of it;

and it shall be presumed conclusively in favour of the Company that every share certificate (if any) so destroyed was a valid certificate duly and properly sealed and that every instrument of transfer so destroyed was a valid and effective instrument duly and properly registered and that every other document destroyed hereunder was a valid and effective document in accordance

with the recorded particulars thereof in the books or records of the Company provided always that:

(a) the foregoing provisions of this Article shall apply only to the destruction of a document in good faith and without express notice to the Company (by a Member or a court) that the preservation of such document was relevant to a claim;

(b) nothing contained in this Article shall be construed as imposing upon the Company any liability in respect of the destruction of any such document earlier than as aforesaid or in any case where the conditions of proviso (a) above are not fulfilled; and

(c) references in this Article to the destruction of any document include references to its disposal in any manner.

WINDING UP

186. If the Company shall be wound up and the assets available for distribution among the Members as such shall be insufficient to repay the whole of the paid up or credited as paid up share capital, such assets shall be distributed so that, as nearly as may be, the losses shall be borne by the Members in proportion to the capital paid up or credited as paid up at the commencement of the winding up on the Shares held by them respectively. If in a winding up the assets available for distribution among the Members shall be more than sufficient to repay the whole of the share capital paid up or credited as paid up at the commencement of the winding up, the excess shall be distributed among the Members in proportion to the capital at the commencement of the winding up paid up or credited as paid up on the said Shares held by them respectively. Notwithstanding the foregoing, this Article shall not affect the rights of the Members holding Shares issued upon special terms and conditions.

186.1. In case of a sale by the liquidator under section 601 of the Companies Act, the liquidator may by the contract of sale agree so as to bind all the Members, for the allotment to the Members directly, of the proceeds of sale in proportion to their respective interests in the Company and may further, by the contract, limit a time at the expiration of which obligations or Shares not accepted or required to be sold shall be deemed to have been irrevocably refused and be at the disposal of the Company, but so that nothing herein contained shall be taken to diminish, prejudice or affect the rights of dissenting Members conferred by the said section.

186.2. The power of sale of the liquidator shall include a power to sell wholly or partially for debentures, debenture stock, or other obligations of another company, either then already constituted or about to be constituted for the purpose of carrying out the sale.

187. If the Company is wound up, the liquidator, with the sanction of a Special Resolution and any other sanction required by the Companies Act, may divide amongst the Members *in specie* or kind the whole or any part of the assets of the Company (whether they shall consist of property of the same kind or not), and, for such purpose, may value any assets and determine how the division shall be carried out as between the Members or different classes of Members. The liquidator, with the like sanction, may vest the whole or any part of such assets in trustees upon such trusts for the benefit of the contributories as, with the like sanction, he or she determines, but so that no Member shall be compelled to accept any assets upon which there is a liability.

INDEMNITY

188.

188.1. Subject to the provisions of, and so far as may be permitted by, the Companies Act, every Director and Secretary shall be entitled to be indemnified by the Company against all costs, charges, losses, expenses and liabilities incurred by him or her in the execution and discharge of his or her duties or in relation thereto, or in his or her capacity as an officer, including any

liability incurred by him in defending any proceedings, civil or criminal, which relate to anything done or omitted or alleged to have been done or omitted by him as a director, an officer or employee of the Company and in which judgement is given in his or her favour (or the proceedings are otherwise disposed of without any finding or admission of any material breach of duty on his or her part) or in which he or she is acquitted or in connection with any application under any statute for relief from liability in respect of any such act or omission in which relief is granted to him by the Court.

188.2. As far as permissible under the Companies Act, the Company shall indemnify any current or former Official (excluding any Director or Secretary in respect only of their role as Director or Secretary of the Company) against expenses, including attorneys' fees, judgments, fines, and amounts paid in settlement actually and reasonably incurred by him or her in connection with any threatened, pending, or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, other than an action by or in the right of the Enterprise in respect of which the Official serves or has served as an Official, to which he or she was, is, or is threatened to be, made a party by reason of the fact that he or she is or was such an Official, provided always that the indemnity contained in this Article 188.2 shall not extend to any matter which would render it void pursuant to the Companies Act.

188.3. In the case of any threatened, pending or completed action, suit or proceeding by or in the right of an Enterprise in respect of which a current or former Official serves or has served, the Company shall indemnify, to the fullest extent permitted by the Companies Act, each person indicated in Article 188.2 against expenses, including attorneys' fees actually and reasonably incurred in connection with the defence or the settlement thereof, except no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable for fraud or dishonesty in the performance of his or her duty to the relevant Enterprise unless and only to the extent that the Court or the court in which such action or suit was brought shall determine upon application that despite the adjudication of liability, but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses as the Court shall deem proper.

188.4. As far as permissible under the Companies Act, expenses, including attorneys' fees, incurred in defending any action, suit or proceeding referred to in this Article shall be paid by the Company in advance of the final disposition of such action, suit or proceeding upon receipt of a written affirmation by or on behalf of the Director, Secretary, Official or other indemnitee of a good faith belief that the criteria for indemnification have been satisfied and a written undertaking to repay such amount if it shall ultimately be determined that he or she is not entitled to be indemnified by the Company as authorised by these Articles.

188.5. It being the policy of the Company that indemnification of the persons specified in this Article shall be made to the fullest extent permitted by law, the indemnification provided by this Article shall not be deemed exclusive (a) of any other rights to which those seeking indemnification or advancement of expenses may be entitled under the Memorandum, Articles, any agreement, any insurance purchased by the Company, any vote of Members or disinterested Directors, or pursuant to the direction (however embodied) of any court of competent jurisdiction, or otherwise, both as to action in his or her official capacity and as to action in another capacity while holding such office, (b) of the power of any Enterprise to indemnify any Official, to the same extent and in the same situations and subject to the same determinations as are hereinabove set forth with respect to a Director, Secretary or Official or (c) of any amendments or replacements of the Companies Act which permit for greater indemnification of the persons specified in this Article and any such amendment or replacement of the Companies Act shall hereby be incorporated into these Articles. As used in this Article 188.5, references to the "Company" include all constituent companies in a consolidation or merger in which the Company or any predecessor to the Company by consolidation or merger was involved. The indemnification provided by this Article shall continue as to a person who has ceased to be a

Director, executive, officer or trustee and shall inure to the benefit of the heirs, executors, and administrators of such a person.

188.6. The Directors shall have power to purchase and maintain for any Director, the Secretary or other officers or employees of the Company insurance against any such liability as referred to in section 235 of the Companies Act and such insurance in respect of Officials as the Directors deem to be appropriate.

188.7. The Company may additionally indemnify any employee or agent of the Company or any director, executive, officer, employee or agent of any of its subsidiaries to the fullest extent permitted by law.

FINANCIAL YEAR

189. The financial year of the Company shall be as prescribed by the Board from time to time.

SHAREHOLDER RIGHTS PLAN

190. The Board is hereby expressly authorised to adopt any shareholder rights plan, or similar plan, agreement or arrangement pursuant to which, under circumstances provided therein, some or all Members will have rights to acquire Shares or interests in Shares, upon such terms and conditions as the Board deems expedient and in the best interests of the Company.

BUSINESS COMBINATION

191.

191.1. The Company may not engage in any business combination, or vote, consent, or otherwise act to authorise a subsidiary of the Company to engage in any business combination, with, with respect to, proposed by or on behalf of, or pursuant to any written or oral agreement, arrangement, relationship, understanding, or otherwise with, any interested Member of the Company or any affiliate or associate of the interested Member for a period of three (3) years following the date that the Member became an interested Member unless:

(a) prior to the date that the Member became an interested Member, the business combination was approved by a committee of the Board formed in accordance with Article 191.3; or

(b) at or following the date that the Member became an interested Member, the business combination is approved by a committee of the Board formed in accordance with Article 191.3 and is authorized by a Special Resolution of the Members. In determining whether the Special Resolution has been adopted by the general meeting, votes cast with respect to Shares of interested Members and their affiliates and associates shall not be taken into account.

191.2. If a good faith definitive proposal regarding a business combination is made in writing to the Board, a committee of the Board formed in accordance with Article 191.3 shall consider and take action on the proposal and respond in writing within thirty (30) days after receipt of the proposal by the Company, setting forth its decision regarding the proposal.

191.3. When a business combination is proposed pursuant to this Article 191, the Board shall promptly form a committee composed solely of one or more disinterested Directors. The committee shall take action on the proposal by the affirmative vote of a majority of committee members. No larger proportion or number of votes shall be required. Notwithstanding anything in these Articles to the contrary, subject to applicable law, the

committee shall not be subject to any direction or control by the Board with respect to the committee's consideration of, or any action concerning, a business combination pursuant to this Article 191. If the Board has no disinterested Directors, the Board shall select three or more disinterested persons to be committee members. Committee members shall act in accordance with the standard of conduct applicable to the Directors and shall be indemnified in accordance with Article 188. For purposes of this Article 191.3, a Director or person is "disinterested" if the Director or person is neither an officer nor an employee, nor has been an officer or employee within five (5) years preceding the formation of the committee pursuant to this Article 191.3, of the Company or of a related company.

191.4. This Article 191 may only be amended by Special Resolution. In determining whether the relevant resolution has been approved by the requisite majority, votes cast with respect to Shares of interested Members and their affiliates and associates shall not be taken into account. Notwithstanding any such amendment, unless determined otherwise by the Board, this Article 191 (as its stands prior to any such amendment) shall apply to any business combination of the Company with an interested Member who became an interested Member before the effective date of the amendment of this Article 191.

191.5. As used in this Article 191 only, the term:

(i) "affiliate" means a person that directly or indirectly controls, is controlled by, or is under common control with, a specified person;

(ii) "associate", when used to indicate a relationship with any person, means any of the following:

(a) any company of which the person is an officer or partner or is, directly or indirectly, the beneficial owner of fifteen percent (15%) or more of any class or series of shares entitled to vote or other equity interest;

(b) any trust or estate in which the person has a substantial beneficial interest or as to which the person serves as trustee or executor or in a similar fiduciary capacity; or

(c) any relative or spouse of the person, or any relative of the spouse, residing in the home of the person;

(iii) "beneficial owner", when used with respect to shares or other securities, includes, but is not limited to, any person who, directly or indirectly through any written or oral agreement, arrangement, relationship, understanding, or otherwise, has or shares the power to vote, or direct the voting of, the shares or securities or has or shares the power to dispose of, or direct the disposition of, the shares or securities, except that:

(a) a person shall not be deemed the beneficial owner of shares or securities tendered pursuant to a tender or exchange offer made by the person or any of the person's affiliates or associates until the tendered shares or securities are accepted for purchase or exchange; and

(b) a person shall not be deemed the beneficial owner of shares or securities with respect to which the person has the power to vote or direct the voting arising solely from a revocable proxy given in response to a proxy solicitation required to be made and made in accordance with the applicable rules and regulations under the Exchange Act and is not then reportable under that act on a Schedule 13D or comparable report, or, if the company is not subject to the rules and regulations under the Exchange Act, would have been required to be made and would not have been reportable if the company had been subject to the rules and regulations;

(iv) "beneficial ownership" includes, but is not limited to, the right to acquire shares or securities through the exercise of options, warrants, or rights, or the conversion of convertible securities, or otherwise. The shares or securities subject to the options, warrants, rights, or conversion privileges held by a person shall be deemed to be outstanding for the purpose of computing the percentage of outstanding shares or securities of the class or series owned by the person, but shall not be deemed to be outstanding for the purpose of computing the percentage of the class or series owned by any other person. A person shall be deemed the beneficial owner of shares and securities beneficially owned by any relative or spouse of the person or any relative of the spouse, residing in the home of the person, any trust or estate in which the person owns fifteen percent (15%) or more of the total beneficial interest or serves as trustee or executor or in a similar fiduciary capacity, any company in which the person owns fifteen percent (15%) or more of the equity, and any affiliate of the person.

When two or more persons act or agree to act as a partnership, limited partnership, syndicate, or other group for the purposes of acquiring, owning, or voting shares or other securities of a company, all members of the partnership, syndicate, or other group are deemed to constitute a "person" and to have acquired beneficial ownership, as of the date they first so act or agree to act together, of all shares or securities of the company beneficially owned by the person;

(v) "business combination" means any of the following:

(a) any merger, acquisition, scheme of arrangement or amalgamation of the Company or any subsidiary of the Company with (1) the interested Member or (2) any other company (whether or not itself an interested Member of the Company) that is, or after the merger would be, an affiliate or associate of the interested Member, but excluding (x) the merger of a wholly owned subsidiary of the Company into the Company, (y) the merger of two or more wholly owned subsidiaries of the Company, or (z) the merger of a company, other than an interested Member or an affiliate or associate of an interested Member, with a wholly owned subsidiary of the Company pursuant to which the surviving company, immediately after the merger, becomes a wholly owned subsidiary of the Company;

(b) any exchange of Shares or other securities of the Company or any subsidiary of the Company or money, or other property, for shares, other securities, money, or property of (1) the interested Member or (2) any other company (whether or not itself an interested Member of the Company) that is, or after the exchange would be, an affiliate or associate of the interested Member, but excluding the exchange of shares of a company, other than an interested Member or an affiliate or associate of an interested Member, pursuant to which the company, immediately after the exchange, becomes a wholly owned subsidiary of the Company;

(c) any sale, lease, exchange, mortgage, pledge, transfer, or other disposition (in a single transaction or a series of transactions), other than sales of goods or services in the ordinary course of business, to or with the interested Member or any affiliate or associate of the interested Member, other than to or with the Company or a wholly owned subsidiary of the Company, of assets of the Company or any subsidiary of the Company (1) having an aggregate market value equal to ten percent (10%) or more of the aggregate market value of all the assets, determined on a consolidated basis, of the Company, (2) having an aggregate market value equal to ten percent (10%) or more of the aggregate market value of all the outstanding Shares of the Company, or (3) representing ten percent (10%) or more of the earning power or net income, determined on a consolidated basis, of the Company, except a cash dividend or distribution paid or made pro rata to all Members of the Company;

(d) the issuance or transfer by the Company or any subsidiary of the Company (in a single transaction or a series of transactions) of any shares of, or other ownership interests in, the Company or any subsidiary of the Company that have an aggregate market value equal to five percent (5%) or more of the aggregate market value of all the outstanding Shares of the Company to the interested Member or any affiliate or associate of the interested Member, except pursuant to the exercise of warrants or rights to purchase shares offered, or a dividend or distribution paid or made, pro rata to all Members of the Company other than for the purpose, directly or indirectly, of facilitating or effecting a subsequent transaction that would have been a business combination if the dividend or distribution had not been made;

(e) the adoption of any plan or proposal for the liquidation or dissolution of the Company, or any reincorporation of the Company in another jurisdiction, proposed by or on behalf of, or pursuant to any written or oral agreement, arrangement, relationship, understanding, or otherwise with, the interested Member or any affiliate or associate of the interested Member;

(f) any reclassification of securities (including, without limitation, any bonus shares or share split, reverse share split, or other distribution of shares in respect of shares), recapitalisation of the Company, merger of the Company with any subsidiary of the Company, exchange of Shares of the Company with any subsidiary of the Company, or other transaction (whether or not with or into or otherwise involving the interested Member), proposed by or on behalf of, or pursuant to any written or oral agreement, arrangement, relationship, understanding, or otherwise with, the interested Member or any affiliate or associate of the interested Member, that has the effect, directly or indirectly, of increasing the proportionate share of the outstanding shares of any class or series of shares entitled to vote, or securities that are exchangeable for, convertible into, or carry a right to acquire shares entitled to vote, of the Company or any subsidiary of the Company that is, directly or indirectly, owned by the interested Member or any affiliate or associate of the interested Member, except as a result of immaterial changes due to fractional share adjustments; or

(g) any receipt by the interested Member or any affiliate or associate of the interested Member of the benefit, directly or indirectly (except proportionately as a Member of the Company), of any loans, advances, guarantees, pledges, or other financial assistance, or any tax credits or other tax advantages provided by or through the Company or any subsidiary of the Company;

(vi) “company” means a corporation, limited liability company, partnership, limited partnership, joint venture, association, business trust, estate, trust, enterprise, and any other legal or commercial entity;

(vii) “control”, including the terms “controlling”, “controlled by”, and “under common control with”, means the possession, directly or indirectly, of the power to direct or cause the direction of the management and policies of a person, whether through the ownership of voting securities, by contract, or otherwise. A person’s beneficial ownership of fifteen percent (15%) or more of the voting power of a company’s outstanding shares entitled to vote in the election of directors creates a presumption that the person has control of the company. Notwithstanding the foregoing, a person is not considered to have control of a company if the person holds voting power, in good faith, as an agent, bank, broker, nominee, custodian, or trustee for one or more beneficial owners who do not individually or as a group have control of the company;

(viii) “governing body” means the body of a company selected by its owners that has the ultimate power to determine the company’s policies and control its activities;

(ix) "interested Member" means any person (including for this purpose any persons acting in concert with that person (as that term is defined in the Takeover Rules issued pursuant to the Irish Takeover Panel Act 1997)) that is (1) the beneficial owner, directly or indirectly, of fifteen percent (15%) or more of the voting power of the outstanding Shares entitled to vote of the Company or (2) an affiliate or associate of the Company that, at any time within the three (3) year period immediately before the date on which it is sought to be determined whether such person is an interested Member, was the beneficial owner, directly or indirectly, of fifteen percent (15%) or more of the voting power of the then outstanding Shares entitled to vote of the Company.

If a person who has not been a beneficial owner of fifteen percent (15%) or more of the voting power of the outstanding Shares entitled to vote of the Company immediately prior to an acquisition of Shares by, or recapitalisation of, the Company or similar action shall become a beneficial owner of fifteen percent (15%) or more of the voting power solely as a result of the share acquisition, recapitalisation, or similar action, the person shall not be deemed to be the beneficial owner of fifteen percent (15%) or more of the voting power for purposes of (1) or (2) above, unless:

(a) the share acquisition, recapitalisation, conversion, or similar action was proposed by or on behalf of, or pursuant to any agreement, arrangement, relationship, understanding, or otherwise (whether or not in writing) with, the person or any affiliate or associate of the person; or

(b) the person thereafter acquires beneficial ownership, directly or indirectly, of outstanding Shares entitled to vote of the Company and, immediately after the acquisition, is the beneficial owner, directly or indirectly, of fifteen percent (15%) or more of the voting power of the outstanding Shares entitled to vote of the Company.

(x) an "interested Member" does not include:

(a) the Company or any of its subsidiaries;

(b) a savings, employee stock ownership, or other employee benefit plan of the Company or its subsidiary, or a fiduciary of the plan when acting in a fiduciary capacity pursuant to the plan; or

(c) a licensed broker/dealer or licensed underwriter who (1) purchases Shares of the Company solely for purposes of resale to the public and (2) is not acting in concert with an interested Member.

Shares beneficially owned by a plan described in clause (b) or by a fiduciary of a plan described in clause (b), pursuant to the plan, are not deemed to be beneficially owned by a person who is a fiduciary of the plan;

(xi) "market value", when used in reference to shares or other property of any company, means the following:

(a) in the case of shares, the average closing sale price of a share during the thirty (30) trading days immediately preceding the date in question:

(1) on the composite tape for Nasdaq Stock Market listed shares; or

(2) if the shares are not quoted on the composite tape or not listed on the Nasdaq Stock Market, on the principal United States securities exchange registered under Exchange Act on which the shares are listed; or

(3) if the shares are not listed on any such exchange, on any system then in use.

If no quotation under clauses (1) through (3) is available, then the market value is the fair market value on the date in question of the shares as determined in good faith by the governing body of the company.

(b) in the case of property other than cash or shares, the fair market value of the property on the date in question as determined in good faith by the governing body of the company.

(xii) "parent" of a specified company means a company that directly, or indirectly through related companies, owns more than fifty percent (50%) of the voting power of the shares or other ownership interests entitled to vote for directors or other members of the governing body of the specified company;

(xiii) "person" includes a natural person and a company;

(xiv) "related company" of a specified company means:

(a) a parent or subsidiary of the specified company;

(b) another subsidiary of a parent of the specified company;

(c) a limited liability company owning, directly or indirectly, more than fifty percent (50%) of the voting power of the shares entitled to vote for directors of the specified company;

(d) a limited liability company having more than fifty percent (50%) of the voting power of its membership interests entitled to vote for members of its governing body owned directly or indirectly by the specified company;

(e) a limited liability company having more than fifty percent (50%) of the voting power of its membership interests entitled to vote for members of its governing body owned directly or indirectly either (1) by a parent of the specified company or (2) a limited liability company owning, directly or indirectly, more than fifty percent (50%) of the voting power of the shares entitled to vote for directors of the specified company; or

(f) a company having more than fifty percent (50%) of the voting power of its shares entitled to vote for directors owned directly or indirectly by a limited liability company owning, directly or indirectly, more than fifty percent (50%) of the voting power of the shares entitled to vote for directors of the specified company;

(xv) "security" means a note, stock, treasury stock, security future, bond, debenture, evidence of indebtedness, certificate of interest or participation in a profit-sharing agreement, collateral trust certificate, preorganization certificate or subscription, transferable share, investment contract, voting trust certificate, certificate of deposit for a security, fractional undivided interest in oil, gas, or other mineral rights, put, call, straddle, option, or privilege on a security, certificate of deposit, or group or index of securities, including an interest therein or based on the value thereof, put, call, straddle, option, or privilege entered into on a national securities exchange relating to foreign currency, or, in general, an interest or instrument commonly known as a "security"; or a certificate of interest or participation in, temporary or interim certificate

for, receipt for, guarantee of, or warrant or right to subscribe to or purchase, any of the foregoing. The term:

(a) includes both a certificated and an uncertificated security;

(b) does not include an insurance or endowment policy or annuity contract under which an insurance company promises to pay a fixed or variable sum of money either in a lump sum or periodically for life or other specified period;

(c) does not include an interest in a contributory or noncontributory pension or welfare plan subject to the United States Employee Retirement Income Security Act of 1974, as amended;

(d) includes as an "investment contract," among other contracts, an interest in a limited partnership and a limited liability company and an investment in a viatical settlement or similar agreement; and

(e) does not include any equity interest of a closely held corporation or other entity with not more than thirty-five (35) holders of the equity interest of such entity offered or sold pursuant to a transaction in which one hundred percent (100%) of the equity interest of such entity is sold as a means to effect the sale of the business of the entity if the transaction has been negotiated on behalf of all purchasers and if all purchasers have access to inside information regarding the entity before consummating the transaction; and

(xvi) "subsidiary" of a specified company means a company having more than fifty percent (50%) of the voting power of its shares or other ownership interests entitled to vote for directors or other members of the governing body of the company owned directly, or indirectly through related companies, by the specified company.

We, the corporate body whose name and address is subscribed, wish to be formed into a company in pursuance of this memorandum of association, and we agree to take the number of shares in the capital of the Company set opposite our respective names.

Name, Address and Description of the Subscriber	Number of shares taken by the Subscriber

For and on behalf of

Dated

Witness to the above signature:

Name:

Address:

Occupation:

Exhibit 5.1

A&L Goodbody

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D01 H104
T +353 1 649 2000
Dx: 29 Dublin | www.algoodbody.com

Dublin
Belfast
London
New York
San Francisco
Palo Alto

Date	16 May 2018
Our Ref	01424577
Your Ref	

Iterum Therapeutics plc
Block 2, Floor 3 Harcourt Centre
Harcourt Street
Dublin 2
Ireland

Re: Iterum Therapeutics plc (the Company)

Dear Sirs

We are acting as Irish counsel to the Company, a public limited company incorporated under the laws of Ireland (registered number 563531), in connection with the initial public offering (the **Transaction**) by the Company of up to 6,133,332 ordinary shares in its capital with a nominal value of US$0.01 per share (the **Ordinary Shares**) pursuant to a registration statement on Form S-1 (File No. 333 224582) originally filed by the Company with the U.S. Securities and Exchange Commission (the **SEC**) on February 2, 2018, as amended (the **Registration Statement**), under the Securities Act of 1933, as amended and the prospectus contained therein (the **Prospectus**, together with the Registration Statement, the **Registration Documents**).

Leerink Partners LLC, RBC Capital Markets, LLC (together the **Representatives**), Guggenheim Securities, LLC and Needham & Company, LLC will act as underwriters to the initial public offering (the **Underwriters**) as will be documented in an underwriting agreement to be entered into between the Company and the Representatives (the **Underwriting Agreement**, and together with the Registration Documents, the **Transaction Documents**).

In connection with the Opinion, we have examined and relied upon copies of:

- the Transaction Documents;
- a copy of the minutes of a meeting of the Board of Directors of the Company held on March 14, 2018;
- a copy of written shareholder resolutions of the Company dated May 15, 2018; and
- a copy of the draft resolutions of the pricing committee of the Board of Directors of the Company to be passed in substantially the same form prior to the Transaction becoming effective.

In addition, we have examined and relied upon:

- legal searches against the Company on May 16, 2018 on the file of the Company maintained by the Registrar of Companies in Dublin, the Judgments Office of the High Court and the Central Office of the High Court (the **Searches**); and

PM Law • CE Gill • EM FitzGerald • JG Grennan • J Coman • PD White • VJ Power • LA Kennedy • SM Doggett • B McDermott • C Duffy • PV Maher • S O'Riordan • MP McKenna • KA Feeney M Sherlock • EP Conlon • E MacNeill • KP Allen • EA Roberts • C Rogers • G O'Toole • JN Kelly • N O'Sullivan • MJ Ward • AC Burke • D Widger • C Christle • S O'Croinin • JW Yarr • DR Baxter A McCarthy • JF Whelan • JB Somerville • MF Barr • AM Curran • A Roberts • M Dale • RM Moore • D Main • J Cahir • M Traynor • PM Murray • N Ryan • P Walker • K Furlong • PT Fahy • M Rasdale D Inverarity • M Coghlan • DR Francis • A Casey • B Hosty • M O'Brien • K Killalea • L Mulleady • K Ryan • E Hurley • G Stanley • D Dagostino • E Keane • C Clarkin • R Grey • R Lyons • J Sheehy • C Morrissey C McLoughlin • C Carroll • SE Carson • P Diggin • J Williams • A O'Beirne • MD Cole • G Conheady • J Dallas • SM Lynch • M McElhinney • C Owens

Consultants: SW Haughey • Professor JCW Wylie • AF Browne • MA Greene • AV Fanagan • JA O'Farrell • IB Moore

- such other corporate records of the Company as we have deemed necessary as a basis for the opinions hereinafter expressed.

Terms not defined herein shall have the meaning respectively assigned to them in the Transaction Documents.

1 Opinion

Subject to the below qualifications and assumptions and to any matters not disclosed to us, we are of the opinion that the issue of the Ordinary Shares, in accordance with the terms of the Registration Statement and the Prospectus, has been duly authorised by all necessary corporate action of the Company and on the allotment and issuance of the Ordinary Shares and the subscription and payment therefor by the relevant subscribers in the manner contemplated by the Registration Statement, the Prospectus and the Underwriting Agreement, the Ordinary Shares will be validly issued, fully paid and non-assessable (which term, when used herein, means that no further sums are required to be paid in connection with the issue of the Ordinary Shares by the holders thereof).

2 Assumptions

For the purposes of giving this Opinion we have assumed:

2.1 the authenticity of all documents submitted to us as originals and the completeness and conformity to the originals of all copies of documents of any kind furnished to us;

2.2 that the copies produced to us of minutes of meetings and/or of resolutions are true copies and correctly record the proceedings of such meetings and/or the subject-matter which they purport to record and that any meetings referred to in such copies were duly convened and held and that all resolutions set out in such minutes were duly passed as described in such minutes and remain in full force and effect;

2.3 the genuineness of the signatures and seals on all original and copy documents which we have examined;

2.4 the truth and accuracy as to factual matters of the contents of the corporate certificate of the Secretary of the Company dated the date of this Opinion;

2.5 that there are no agreements or arrangements in existence which in any way amend or vary the terms of the Transaction;

2.6 the accuracy and completeness of all information appearing on public records;

2.7 the accuracy and completeness of the information disclosed in the Searches and that such information is accurate as of the date of this opinion and has not since the time of such search or enquiry been altered;

2.8 that there has been no alteration in the status or condition of the Company as disclosed by the Searches;

2.9 the absence of fraud on the part of the Company and its respective officers, employees, agents and advisers and that the Company has entered into the Transaction in good faith, for its legitimate business purposes, for good consideration, and that it derives commercial benefit from the Transaction commensurate with the risks undertaken by it in the Transaction;

2.10 that any Ordinary Shares offered under the Registration Statement will be in consideration of the receipt by the Company prior to the issue of the Ordinary Shares pursuant thereto of either cash or the release of a liability of the Company for a liquidated sum, at least equal to the nominal value of such Ordinary Shares and any premium required to be paid up on the Ordinary Shares pursuant to their terms of issue;

2.11 that all securities issued and sold under the Registration Statement will be issued and sold in compliance with all applicable laws (other than Irish law), including applicable federal and state securities laws, in the manner stated in the Registration Statement and the appropriate prospectus supplement;

2.12 that the Underwriting Agreement will have been duly authorised and validly executed and delivered by the Company and the other parties thereto;

2.13 that, at the time of issue of the Ordinary Shares, the authority of the Company and the directors of the Company to issue the Ordinary Shares, as provided for in the Irish Companies Act 2014 (the Companies Act) and the Constitution of the Company, is in full force and effect;

2.14 that the issue of the Ordinary Shares will be in compliance with the Companies Act, the Irish Takeover Panel Act, 1997, Takeover Rules 2013, and all other applicable Irish company, takeover, securities, market abuse, insider dealing laws and other rules and regulations;

2.15 that, as at the time of the issuance of the Ordinary Shares, such issuance shall not be in contravention or breach of any agreement, undertaking, arrangement, deed or covenant affecting the Company or to which the Company is a party or otherwise bound or subject; and

2.16 that the Registration Documents do not constitute (and are not intended/required to constitute) a prospectus within the meaning of Part 23 of the Companies Act and that no offer of securities to the public is made, or will be made, that required the publication of a prospectus pursuant to Irish prospectus law in general, or in particular pursuant to the Prospectus (Directive 2003/71/EC) Regulations 2005 of Ireland (as amended).

In rendering this Opinion we have confined ourselves to matters of Irish law. We express no opinion on any laws other than the laws of Ireland (and the interpretation thereof) in force as at the date hereof. This Opinion speaks only as of its date. We are not under any obligation to update this Opinion from time to time, nor to notify you of any change of law, facts or circumstances referred to or relied upon in the giving of this Opinion.

This Opinion is given solely for the benefit of the addressee of this Opinion and may not be relied upon by any other person without our prior written consent, provided, however, that it may be relied upon by persons entitled to rely on it pursuant to applicable provisions of US federal securities laws.

This Opinion is also strictly confined to the matters expressly stated herein and is not to be read as extending by implication or otherwise to any other matter.

We hereby consent to the filing of this Opinion with the SEC as an exhibit to the Registration Statement and any amendments thereto and to the use of our name therein under the caption “Legal Matters”.

The Opinion is governed by and construed in accordance with the laws of Ireland.

Yours faithfully

/s/ A&L Goodbody

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY

2018 EQUITY INCENTIVE PLAN

1. GENERAL.

(a) Relationship to Prior Plan.

(i) This Plan is intended as the successor to the Iterum Therapeutics Public Limited Company (formerly Iterum Therapeutics Limited) 2015 Equity Incentive Plan (the "***Prior Plan***") with respect to grants to Employees. From and after 12:01 a.m. Central time on the IPO Date, no additional awards will be granted under the Prior Plan, and any shares that would otherwise remain available for future grants under the Prior Plan as of 12:01 a.m. Central time on the IPO Date will cease to be available under the Prior Plan at such time. All Awards granted on or after 12:01 a.m. Central time on the IPO Date will be granted under this Plan. All awards granted under the Prior Plan will remain subject to the terms of the Prior Plan.

(ii) From and after 12:01 a.m. Central time on the IPO Date, any shares subject, at such time, to outstanding stock awards granted under the Prior Plan that (i) are no longer required to satisfy such awards because the awards will expire or terminate for any reason prior to exercise or settlement; (ii) are forfeited because of the failure to meet a contingency or condition required to vest such shares or otherwise return to the Company; or (iii) subject to compliance with Irish company law are reacquired, withheld (or not issued) to satisfy a tax withholding obligation in connection with an award or to satisfy the purchase price or exercise price of a stock award (such shares the "***Returning Shares***") will immediately be added to the Share Reserve (as further described in Section 3(a) below) as and when such shares become Returning Shares, up to the maximum number set forth in Section 3(a) below.

(b) Eligible Award Recipients. The persons eligible to receive Awards are Employees.

(c) Available Awards. The Plan provides for the grant of the following Awards: (i) Incentive Stock Options, (ii) Nonstatutory Stock Options, (iii) Stock Appreciation Rights (iv) Restricted Stock Awards, (v) Restricted Stock Unit Awards, (vi) Performance Stock Awards, (vii) Performance Cash Awards, and (viii) Other Stock Awards.

(d) Purpose. The Plan, through the grant of Awards, is intended to help the Company secure and retain the services of eligible award recipients, provide incentives for such persons to exert maximum efforts for the success of the Company and any Affiliate and provide a means by which the eligible recipients may benefit from increases in value of the Ordinary Shares.

(a) Definitions. All capitalized terms in this document are defined in Section 13 below.

2. ADMINISTRATION.

(a) Administration by the Board. The Board will administer the Plan. The Board may delegate administration of the Plan to a Committee or Committees, as provided in Section 2(c). In addition, the Board or a Committee may appoint a Stock Plan Administrator with the authority to administer the day to day operations of the Plan, and to make decisions with respect to the Plan and Awards.

(b) Powers of the Board. The Board will have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine from time to time (A) which of the persons eligible under the Plan will be granted Awards; (B) when and how each Award will be granted; (C) what type or combination of types of Award will be granted; (D) the provisions of each Award granted (which need not be identical), including the time or times when a person will be permitted to exercise or otherwise receive cash or Ordinary Shares under the Stock Award; (E) the number of Ordinary Shares with respect to which a Stock Award shall be granted to each such person; and (F) the Fair Market Value applicable to a Stock Award.

(ii) To construe and interpret the Plan and Awards granted under it, to establish, amend and revoke rules and regulations for its administration, and to settle all controversies regarding the Plan and Awards granted under it. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Award Agreement or in the written terms of a Performance Cash Award, in a manner and to the extent it will deem necessary or expedient to make the Plan or Award fully effective.

(iii) To prohibit (or delegate to the Stock Plan Administrator the authority to prohibit) the exercise of any Option, SAR or other exercisable Award during a period of up to thirty days prior to the consummation of any pending share dividend, share split, combination or exchange of shares, merger, consolidation or other distribution (other than normal cash dividends) of Company assets to shareholders, or any other change affecting the Ordinary Shares or the share price of the Ordinary Shares, including any Corporate Transaction, for reasons of administrative convenience.

(iv) To accelerate the time at which an Award may be exercised or the time during which an Award or any part thereof will vest.

(v) To approve forms of Award Agreements for use under the Plan and to amend the terms of any one or more Awards, subject to any specified limits in the Plan that are not subject to Board discretion; *provided however*, that a Participant's rights under any Award will not be materially impaired by any such amendment unless (A) the Company requests the consent of the affected Participant, and (B) such Participant consents in writing. Notwithstanding the foregoing, and subject to the limitations of applicable law, if any, the Board may amend the terms of any one or more Awards without the affected Participant's consent (w) to maintain the qualified status of the Award as an Incentive Stock Option under Section 422 of the Code; (x) to change the terms of an Incentive Stock Option, if such change results in impairment of the Stock Award solely because it impairs the qualified status of the Stock Award as an Incentive Stock Option under Section 422 of the Code; (y) to clarify the manner of exemption from, or to bring the Award into compliance with, Section 409A of the Code; or (z) to comply with other applicable laws.

(vi) To amend, suspend or terminate the Plan as provided by Section 10.

(vii) To effect, with the consent of any adversely affected Participant, (A) the alteration of the exercise, purchase or strike price of any outstanding Stock Award (unless this is in the context of a Capitalization Adjustment in which case Participant consent is not required); (B) the cancellation of any outstanding Stock Award and the grant in substitution therefor of a new (1) Option or SAR, (2) Restricted Stock Award, (3) Restricted Stock Unit Award, (4) Other Stock Award, (5) cash and/or (6) other valuable consideration determined by the Board, in its sole discretion, with any such substituted award (x) covering the same or a different number of Ordinary Shares as the cancelled Stock Award and (y) granted under the Plan or another equity or compensatory plan of the Company; or (C) any other action that is treated as a repricing under generally accepted accounting principles.

(viii) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and any Affiliates and that are not in conflict with the provisions of the Plan or Awards.

(c) Delegation to Committee. The Board may delegate some or all of the administration of the Plan to a Committee or Committees. If administration of the Plan is delegated to a Committee, the Committee will have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee of the Committee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board will thereafter be to the Committee or subcommittee, as applicable). Any delegation of administrative powers will be reflected in resolutions, not inconsistent with the provisions of the Plan, adopted from time to time by the Board or Committee (as applicable). The Board may retain the authority to concurrently administer the Plan with the Committee and may, at any time, revest in the Board some or all of the powers previously delegated. The Committee may consist solely of two or more Non-Employee Directors, in accordance with Rule 16b-3.

(d) Delegation to an Officer. Subject to compliance with Irish law, the Board may delegate to one or more Officers the authority to do one or both of the following: (i) designate Employees who are providing Continuous Service to the Company or any of its Subsidiaries who are not Officers to be recipients of Stock Awards and the terms thereof, and (ii) determine the number of Ordinary Shares to be subject to such Stock Awards granted to such Employees; *provided, however*, that the Board resolutions regarding such delegation shall specify the total number of Ordinary Shares that may be subject to the Stock Awards granted by such Officer and that such Officer may not grant a Stock Award to himself or herself. Notwithstanding the foregoing, the Board may not delegate authority to an Officer to determine the Fair Market Value of the Ordinary Shares.

(e) Effect of Board's Decision. All determinations, interpretations and constructions made by the Board in good faith will not be subject to review by any person and will be final, binding and conclusive on all persons.

3. SHARES SUBJECT TO THE PLAN.

(a) Share Reserve.

(i) Subject to the provisions of this Section 3(a), and Section 9(a) relating to Capitalization Adjustments, the aggregate number of Ordinary Shares reserved for issuance pursuant to Stock Awards from and after the IPO Date is 1,018,459 shares (the "***Share Reserve***"), which number shall *include* (i) any shares remaining for issuance pursuant to the Prior Plan as of the IPO Date and (ii) any Returning Shares.

(ii) In addition, the Board may approve an increase on January 1st of each year for a period of not more than ten (10) years commencing on January 1, 2019 and ending on (and including) January 1, 2028 of an amount up to 4% of the total number of Ordinary Shares outstanding on December 31st of the preceding calendar year. For clarity, the limit in this Section 3(a) is a limit on the number of Ordinary Shares that may be issued pursuant to the Plan. Accordingly, this Section 3(a) does not limit the granting of Stock Awards except as provided in Section 7(a).

(iii) In addition, subject to compliance with Irish law shares may be issued in connection with a merger or acquisition as permitted by, as applicable, NASDAQ Marketplace Rule 4350(i)(1)(A)(iii), NYSE Listed Company Manual Section 303A.08, AMEX Company Guide Section 711 or other applicable stock exchange rules, and such issuance shall not reduce the number of Ordinary Shares available for issuance under the Plan.

(b) Reversion of Shares to the Share Reserve. If subject to compliance with Irish law (i) any Ordinary Shares issued pursuant to a Stock Award are forfeited back to or repurchased by the Company or any Affiliate because of the failure to meet a contingency or condition required for the vesting of such Ordinary Shares, or (ii) any Ordinary Shares are cancelled in accordance with the cancellation and regrant provisions of Section 2(b)(x), then the Ordinary Shares that are forfeited, repurchased or canceled shall revert to and again become available for issuance under the Plan. If any Ordinary Shares subject to a Stock Award are not delivered to a Participant because such Ordinary Shares are withheld for the payment of taxes pursuant to Section 8(g) or a Stock Award is exercised through a reduction of Ordinary Shares subject to the Stock Award (*i.e*., "net exercised") or an appreciation distribution in respect of a Stock Appreciation Right is paid in Ordinary Shares, the number of Ordinary Shares subject to the Stock Award that are not delivered to the Participant shall remain available for subsequent issuance under the Plan. If the exercise price of any Stock Award is satisfied by tendering Ordinary Shares held by the Participant (either by actual delivery or attestation), then the number of Ordinary Shares so tendered shall remain available for issuance under the Plan.

(c) Incentive Stock Option Limit. Subject to the limit in Section 3(a), and Section 9(a) relating to Capitalization Adjustments, the aggregate maximum number of Ordinary Shares that may be issued pursuant to the exercise of Incentive Stock Options will be a number of Ordinary Shares equal to three (3) times the Share Reserve as of the IPO Date.

(d) Source of Shares. The Ordinary Shares issuable under the Plan shall be authorized but unissued or reacquired Ordinary Shares, including Ordinary Shares redeemed or repurchased by the Company or any Affiliate on the open market or otherwise, in accordance with applicable Irish law.

4. ELIGIBILITY.

(a) Eligibility for Specific Stock Awards. Incentive Stock Options may be granted only to employees of the Company or a "parent corporation" or "subsidiary corporation" thereof (as such terms are defined in Sections 424(e) and 424(f) of the Code). Stock Awards other than Incentive Stock Options may be granted to any Employee.

(b) Ten Percent Shareholders. A Ten Percent Shareholder will not be granted an Incentive Stock Option unless the exercise price of such Option is at least 110% of the Fair Market Value on the date of grant and the Option is not exercisable after the expiration of five (5) years from the date of grant.

5. PROVISIONS RELATING TO OPTIONS AND STOCK APPRECIATION RIGHTS.

Each Option or SAR will be in such form and will contain such terms and conditions as the Board deems appropriate. All Options will be separately designated Incentive Stock Options or Nonstatutory Stock Options at the time of grant, and, if certificates are issued, a separate certificate or certificates will be issued for Ordinary Shares purchased on exercise of each type of Option. If an Option is not specifically designated as an Incentive Stock Option, or if an Option is designated as an Incentive Stock Option but some portion or all of the Option fails to qualify as an Incentive Stock Option under the applicable rules, then the Option (or portion thereof) will be a Nonstatutory Stock Option. The provisions of separate Options or SARs need not be identical; *provided, however*, that each Award Agreement will conform to (through incorporation of provisions hereof by reference in the applicable Award Agreement or otherwise) the substance of each of the following provisions:

(a) Term. Subject to the provisions of Section 4(b) regarding Ten Percent Shareholders, no Option or SAR will be exercisable after the expiration of 10 years from the date of its grant or such shorter period specified in the Award Agreement.

(b) Exercise Price. Subject to the provisions of Section 4(b) regarding Ten Percent Shareholders, the exercise or strike price of each Award will be not less than the greater of (i) the nominal value of an Ordinary Share or (ii) 100% of the Fair Market Value of the Ordinary Shares subject to the Option or SAR on the date the Stock Award is granted. Notwithstanding the foregoing, an Option or SAR may be granted with an exercise or strike price lower than 100% of the Fair Market Value of the Ordinary Shares subject to the Award if such Award is granted pursuant to an assumption of or substitution for another option or stock appreciation right pursuant to a Corporate Transaction and in a manner consistent with the provisions of Section 409A of the Code and, if applicable, Section 424(a) of the Code, provided that in all cases it will not be less than the nominal value of an Ordinary Share. Each SAR will be denominated in Ordinary Share equivalents.

(c) Exercise and Purchase Price for Options. To exercise any outstanding Option, the Participant must provide written notice of exercise to the Company in the manner determined by the Stock Plan Administrator. The purchase price of Ordinary Shares acquired pursuant to the exercise of an Option may be paid, to the extent permitted by applicable law and as determined by the Board in its sole discretion, by any combination of the methods of payment set forth below. The Board will have the authority to grant Options that do not permit all of the following methods of payment (or otherwise restrict the ability to use certain methods) and to grant Options that require the consent of the Company to use a particular method of payment. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share is fully paid up. The permitted methods of payment are as follows:

(i) by cash, check, bank draft or money order payable to the Company;

(ii) pursuant to a program developed under Regulation T as promulgated by the U.S. Federal Reserve Board that, prior to the issuance of Ordinary Shares subject to the Option, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds;

(iii) by delivery to the Company (either by actual delivery or attestation) of Ordinary Shares;

(iv) if the option is a Nonstatutory Stock Option, by a "net exercise" arrangement pursuant to which the Company will reduce the number of Ordinary Shares issuable upon exercise by the largest whole number of Ordinary Shares with a Fair Market Value that does not exceed the aggregate exercise price; *provided, however*, that:

(1) the Company will accept a cash or other payment from the Participant to the extent of any remaining balance of the aggregate exercise price not satisfied by such reduction in the number of whole Ordinary Shares to be issued;

(2) irrespective of whether a "net exercise" arrangement is used, the nominal value of each newly issued Ordinary Shares will be fully paid up in cash; and

(3) Ordinary Shares will no longer be subject to an Option and will not be exercisable thereafter to the extent that (A) Ordinary Shares issuable upon exercise are used to pay the exercise price pursuant to the "net exercise," (B) Ordinary Shares are delivered to the Participant as a result of such exercise, and (C) Ordinary Shares are withheld to satisfy tax withholding obligations;

(v) deduction from salary due and payable to an Employee by the Company or any Affiliate; or

(vi) in any other form of legal consideration that may be acceptable to the Board or the Stock Plan Administrator and permissible under applicable law.

(d) Exercise and Payment of a SAR. To exercise any outstanding SAR, the Participant must provide written notice of exercise to the Company in compliance with the provisions of the Award Agreement evidencing such SAR. The appreciation distribution payable on the exercise of a SAR will be not greater than an amount equal to the excess of (A) the aggregate Fair Market Value (on the date of the exercise of the SAR) of a number of Ordinary Shares equal to the number of Ordinary Shares equivalents in which the Participant is vested under such SAR, and with respect to which the Participant is exercising the SAR on such date, over (B) the aggregate strike price of the number of Ordinary Shares equivalents with respect to which the Participant is exercising the SAR on such date . The appreciation distribution may be paid in Ordinary Shares, in cash, in any combination of the two or in any other form of consideration, as determined by the Board and contained in the Award Agreement evidencing such SAR. Where the SAR is settled using newly issued Ordinary Shares the Company shall require that the nominal value of each newly issued Ordinary Share is fully paid up.

(e) Transferability of Options and SARs. The Board may, in its sole discretion, impose such limitations on the transferability of Options and SARs as the Board will determine. In the absence of such a determination by the Board to the contrary, the following restrictions on the transferability of Options and SARs will apply:

(i) Restrictions on Transfer. An Option or SAR will not be transferable except by will or by the laws of descent and distribution (or pursuant to subsections (ii) and (iii) below), and will be exercisable during the lifetime of the Participant only by the Participant; *provided, however*, that the Board or the Stock Plan Administrator may, in its sole discretion, permit transfer of the Option or SAR in a manner that is not prohibited by applicable tax and securities laws upon the Participant's request. Except as explicitly provided in the Plan, neither an Option nor a SAR may be transferred for consideration.

(ii) Domestic Relations Orders. Subject to the approval of the Board or the Stock Plan Administrator, an Option or SAR may be transferred pursuant to the terms of a domestic relations order, official marital settlement agreement or other divorce or separation instrument which contains the information required by the Company to effect the transfer. If an Option is an Incentive Stock Option, such Option may be deemed to be a Nonstatutory Stock Option as a result of such transfer.

(iii) Beneficiary Designation. Subject to the approval of the Board or the Stock Plan Administrator, a Participant may, by delivering written notice to the Company, in a form provided by or otherwise satisfactory to the Stock Plan Administrator and any broker designated by the Company to effect Option exercises, designate a third party who, in the event of the death of the Participant, will thereafter be entitled to exercise the Option or SAR and receive the Ordinary Shares or other consideration resulting from such exercise. In the absence of such a designation, upon the death of the Participant, the executor or administrator of the Participant's estate will be entitled to exercise the Option

or SAR and receive the Ordinary Shares or other consideration resulting from such exercise in accordance with the Participants will or the laws of intestacy as applicable. However, the Company may prohibit designation of a beneficiary at any time, including due to any conclusion by the Company that such designation would be inconsistent with the provisions of applicable laws whether in the United States or any other jurisdiction in which a Participant resides.

(f) Vesting Generally. The total number of Ordinary Shares subject to an Option or SAR may vest and therefore become exercisable in periodic installments that may or may not be equal. The Option or SAR may be subject to such other terms and conditions on the time or times when it may or may not be exercised (which may be based on the satisfaction of Performance Goals or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options or SARs may vary. The provisions of this Section 5(f) are subject to any Option or SAR provisions governing the minimum number of Ordinary Shares as to which an Option or SAR may be exercised.

(g) Termination of Continuous Service. If a Participant's Continuous Service terminates, the Participant may exercise his or her Option or SAR (to the extent that the Participant was entitled to exercise the vested portion of such Award as of the date of termination of Continuous Service) but only within such period of time following the termination of the Participant's Continuous Service as set forth in the Award Agreement. Unless otherwise provided in the Award Agreement, the Option or SAR will be exercisable for a period of three (3) months following a termination of a Participant's Continuous Service by the Company without Cause or by the Participant for any reason; *provided, however* that such post-termination exercise period will instead be for the twelve (12) month period following a termination due to the Participant's Disability or death. Additionally, if the Participant's death occurs within the applicable post-termination of Continuous Service period during which the Option was exercisable, the Option will be exercisable for a twelve (12) month period following the Participant's death. If, after termination of Continuous Service, the Participant does not exercise his or her Option or SAR prior to the applicable deadline the Option or SAR will terminate.

(h) Automatic Extension of Termination Date. If the exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than for Cause and other than upon the Participant's death or Disability) would be prohibited at any time solely because the issuance of Ordinary Shares would violate the registration requirements under the Securities Act, then the Option or SAR will terminate on the earlier of (i) the expiration of a total period of time (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the exercise of the Option or SAR would not be in violation of such registration requirements, and (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement. In addition, unless otherwise provided in a Participant's Award Agreement, if the sale of any Ordinary Shares received upon exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than for Cause) would violate the Company's insider trading policy, then the Option or SAR will terminate on the earlier of (i) the expiration of the period of time (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the sale of the Ordinary Shares received upon exercise of the Option or SAR would not be in violation of the Company's insider trading policy, and (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement.

(i) Termination for Cause. Except as explicitly provided otherwise in a Participant's Award Agreement or other individual written agreement between the Company or any Affiliate and the Participant, if a Participant's Continuous Service is terminated for Cause, the Option or SAR will terminate immediately upon such Participant's termination of Continuous Service, and the Participant will be prohibited from exercising his or her Option or SAR from and after the date of such termination of Continuous Service.

(j) Non-Exempt Employees under U.S. Law. If an Option or SAR is granted to an Employee who is a non-exempt employee for purposes of the U.S. Fair Labor Standards Act of 1938, as amended, the Option or SAR will not be first exercisable for any Ordinary Shares until at least six months following the date of grant of the Option or SAR (although the Award may vest prior to such date). Consistent with the provisions of the U.S. Worker Economic Opportunity Act, (i) if such non-exempt Employee dies or suffers a Disability, (ii) upon a Corporate Transaction in which such Option or SAR is not assumed, continued, or substituted, (iii) upon a Change in Control, or (iv) upon the Participant's retirement (as such term may be defined in the Participant's Award Agreement in another agreement between the Participant and the Company, or, if no such definition, in accordance with the Company's then current employment policies and guidelines), the vested portion of any Options and SARs may be exercised earlier than six months following the date of grant. The foregoing provision is intended to operate so that any income derived by a non-exempt employee in connection with the exercise or vesting of an Option or SAR will be exempt from his or her regular rate of pay. To the extent permitted and/or required for compliance with the U.S. Worker Economic Opportunity Act to ensure that any income derived by a non-exempt employee in connection with the exercise, vesting or issuance of any shares under any other Stock Award will be exempt from the employee's regular rate of pay, the provisions of this Section 5(j) will apply to all Stock Awards and are hereby incorporated by reference into such Award Agreements.

(k) Incentive Stock Option Limitations. To the extent that the aggregate Fair Market Value (determined at the time of grant) of an Ordinary Share with respect to which Incentive Stock Options are exercisable for the first time by any Participant during any calendar year (under all plans of the Company and any Affiliates) exceeds U.S. $100,000 (or such other limit established in the Code) or otherwise does not comply with the rules governing Incentive Stock Options, the Options or portions thereof that exceed such limit (according to the order in which they were granted) or otherwise do not comply with such rules will be treated as Nonstatutory Stock Options, notwithstanding any contrary provision of an applicable Award Agreement.

(l) Whole Shares. Options and SARs may be exercised only with respect to whole shares.

6. PROVISIONS OF STOCK AWARDS OTHER THAN OPTIONS AND SARS.

(a) Restricted Stock Awards. Each Restricted Stock Award will be in such form and will contain such terms and conditions as the Board will deem appropriate. To the extent consistent with the Company's Constitution, at the Board's election, Ordinary Shares underlying a Restricted Stock Award may be (i) held in book entry form subject to the Company's instructions until any restrictions relating to the Restricted Stock Award lapse; or (ii) evidenced by a certificate, which certificate will be held in such form and manner as determined by the Board. The terms and conditions of Restricted Stock Awards may change from time to time, and the terms and conditions of separate Restricted Stock Awards need not be identical; *provided, however*, that each Award Agreement will conform to (through incorporation of the provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. A Restricted Stock Award may be awarded in consideration for (A) cash, check, bank draft or money order payable to the Company, (B) past services to the Company or an Affiliate, or (C) any other form of legal consideration (including future services) that may be acceptable to the Board, in its sole discretion, and permissible under applicable law. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share issued in satisfaction of a Restricted Stock Award is fully paid up.

(ii) Vesting. Ordinary Shares awarded under a Restricted Stock Award may be subject to forfeiture to the Company in accordance with a vesting schedule to be determined by the Board and subject to compliance with Irish law.

(iii) Termination of Participant's Continuous Service. If a Participant's Continuous Service terminates, the Company may receive through a forfeiture condition or a repurchase right subject to compliance with Irish law, any or all of the Ordinary Shares held by the Participant that have not vested as of the date of termination of Continuous Service under the terms of the Award Agreement.

(iv) Transferability. Rights to acquire Ordinary Shares under the Restricted Stock Award will be transferable by the Participant only upon such terms and conditions as are set forth in the Award Agreement, as the Board will determine in its sole discretion, so long as Ordinary Shares awarded under the Restricted Stock Award remain subject to the terms of the Award Agreement.

(v) Dividends. An Award Agreement may provide that any dividends paid on Restricted Stock will be subject to the same vesting and forfeiture restrictions as apply to the shares subject to the Restricted Stock Award to which they relate.

(b) Restricted Stock Unit Awards. Each Restricted Stock Unit Award will be in such form and will contain such terms and conditions as the Board will deem appropriate. The terms and conditions of Restricted Stock Unit Awards may change from time to time, and the terms and conditions of separate Restricted Stock Unit Awards need not be identical; *provided* that each Restricted Stock Unit Award Agreement will conform to (through incorporation of the provisions hereof by reference in the Agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. At the time of grant of a Restricted Stock Unit Award, the Board will determine the consideration, if any, to be paid by the Participant upon delivery of each share of Ordinary Shares subject to the Restricted Stock Unit Award. The consideration to be paid (if any) by the Participant for each share of Ordinary Shares subject to a Restricted Stock Unit Award may be paid in any form of legal consideration that may be acceptable to the Board, in its sole discretion, and permissible under applicable law.

(ii) Vesting. At the time of the grant of a Restricted Stock Unit Award, the Board may impose such restrictions on or conditions to the vesting of the Restricted Stock Unit Award as it, in its sole discretion, deems appropriate.

(iii) Payment. A Restricted Stock Unit Award may be settled by the delivery of Ordinary Shares, their cash equivalent, any combination thereof or in any other form of consideration, as determined by the Board and contained in the Restricted Stock Unit Award Agreement. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share issued in satisfaction of a Restricted Stock Unit Award is fully paid up.

(iv) Additional Restrictions. At the time of the grant of a Restricted Stock Unit Award, the Board, as it deems appropriate, may impose such restrictions or conditions that delay the delivery of the Ordinary Shares (or their cash equivalent) subject to a Restricted Stock Unit Award to a time after the vesting of such Restricted Stock Unit Award.

(v) Dividend Equivalents. Dividend equivalents may be credited in respect of Ordinary Shares covered by a Restricted Stock Unit Award, as determined by the Board and contained in the Restricted Stock Unit Award Agreement. At the sole discretion of the Board, such dividend equivalents may be converted into additional Ordinary Shares covered by the Restricted Stock Unit Award in such manner as determined by the Board. Any additional Ordinary Shares covered by the Restricted Stock Unit Award credited by reason of such dividend equivalents will be subject to all of the same terms and conditions of the underlying Award Agreement to which they relate.

(vi) Termination of Participant's Continuous Service. Except as otherwise provided in the applicable Award Agreement, such portion of the Restricted Stock Unit Award that has not vested will be forfeited upon the Participant's termination of Continuous Service.

(c) Performance Awards.

(i) Performance Stock Awards. A Performance Stock Award is a Stock Award that may vest or may be exercised contingent upon the attainment during a Performance Period of certain Performance Goals. A Performance Stock Award may, but need not, require the completion of a specified period of Continuous Service. The length of any Performance Period, the Performance Goals to be achieved during the Performance Period, and the measure of whether and to what degree such Performance Goals have been attained shall be conclusively determined by the Committee, in its sole discretion. The Board may provide for or, subject to such terms and conditions as the Board may specify, may permit a Participant to elect for, the payment of any Performance Stock Award to be deferred to a specified date or event. In addition, to the extent permitted by applicable law and the applicable Award Agreement, the Board may determine that cash may be used in payment of Performance Stock Awards.

(ii) Performance Cash Awards. A Performance Cash Award is a cash award that may be paid contingent upon the attainment during a Performance Period of certain Performance Goals. A Performance Cash Award may also require the completion of a specified period of Continuous Service. At the time of grant of a Performance Cash Award, the length of any Performance Period, the Performance Goals to be achieved during the Performance Period, and the measure of whether and to what degree such Performance Goals have been attained shall be conclusively determined by the Committee, in its sole discretion. The Committee may specify the form of payment of Performance Cash Awards, which may be cash or other property, or may provide for a Participant to have the option for his or her Performance Cash Award, or such portion thereof as the Board may specify, to be paid in whole or in part in cash or other property.

(iii) Board Discretion. The Board retains the discretion to amend the compensation or economic benefit due upon attainment of Performance Goals and to define the manner of calculating the Performance Criteria it selects to use for a Performance Period.

(d) Other Stock Awards. Other forms of Stock Awards valued in whole or in part by reference to, or otherwise based on, Ordinary Shares, including the appreciation in value thereof (e.g., options or share rights with an exercise price or strike price less than 100% of the Fair Market Value of the Ordinary Shares at the time of grant) may be granted either alone or in addition to Stock Awards provided for under Section 5 and the preceding provisions of this Section 6. Subject to the provisions of the Plan, the Board will have sole and complete authority to determine the persons to whom and the time or times at which such Other Stock Awards will be granted, the number of Ordinary Shares (or the cash equivalent thereof) to be granted pursuant to such Other Stock Awards and all other terms and conditions of such Other Stock Awards; *provided, however,* that where Ordinary Shares are issued pursuant to any Other Stock Award, the nominal value of each newly issued Ordinary Share is fully paid up.

7. COVENANTS OF THE COMPANY.

(a) Availability of Shares. During the terms of the Stock Awards, the Company shall keep available at all times the authorized but unissued Ordinary Shares reasonably required to satisfy such Stock Awards.

(b) Securities Law Compliance. The Company will seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell Ordinary Shares upon exercise of the Stock Awards; *provided, however*, that this undertaking will not require the Company to register under the Securities Act, the Plan, any Stock Award or any Ordinary Shares issued or issuable pursuant to any such Stock Award. If, after reasonable efforts and at a reasonable cost, the Company is unable to obtain from any such regulatory commission or agency the authority that counsel for the Company deems necessary for the lawful issuance and sale of Ordinary Shares under the Plan, the Company will be relieved from any liability for failure to issue and sell Ordinary Shares upon exercise of such Stock Awards unless and until such authority is obtained. A Participant will not be eligible for the grant of a Stock Award or the subsequent issuance of cash or Ordinary Shares pursuant to the Stock Award if such grant or issuance would be in violation of any applicable securities law.

(c) No Obligation to Notify or Minimize Taxes. The Company and its Affiliates shall have no duty or obligation to any Participant to advise such holder as to the time or manner of exercising such Stock Award. Furthermore, the Company and its Affiliates shall have no duty or obligation to warn or otherwise advise such holder of a pending termination or expiration of a Stock Award or a possible period in which the Stock Award may not be exercised. The Company and its Affiliates have no duty or obligation to minimize the tax consequences of a Stock Award to the holder of such Stock Award.

8. GENERAL TERMS OF AWARDS.

(a) Use of Proceeds from Sales of Ordinary Shares. Proceeds from the sale of Ordinary Shares pursuant to Stock Awards will constitute general funds of the Company.

(b) Corporate Action Constituting Grant of Stock Awards. Corporate action constituting a grant by the Company of a Stock Award to any Participant will be deemed completed as of the date of such corporate action, unless otherwise determined by the Board, regardless of when the instrument, certificate, or letter evidencing the Stock Award is communicated to, or actually received or accepted by, the Participant. In the event that the corporate records (e.g., Board consents, resolutions or minutes) documenting the corporate action constituting the grant contain terms (e.g., exercise price, vesting schedule or number of shares) that are inconsistent with those in the Award Agreement or related grant documents as a result of a clerical error in the papering of the Award Agreement or related grant documents, the corporate records will control and the Participant will have no legally binding right to the incorrect term in the Award Agreement or related grant documents.

(c) Shareholder Rights. No Participant will be deemed to be the holder of, or to have any of the rights of a holder with respect to, any Ordinary Shares subject to a Stock Award unless and until (i) such Participant has satisfied all requirements for exercise of, or the issuance of Ordinary Shares under, the Stock Award pursuant to its terms, and (ii) the issuance of the Ordinary Shares subject to the Stock Award has been entered into the books and records of the Company.

(d) No Employment or Other Service Rights. Nothing in the Plan, any Award Agreement or any other instrument executed thereunder or in connection with any Award granted pursuant thereto will confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Award was granted or will affect any right that the Company or an Affiliate may have to terminate (i) the employment of an Employee with or without notice and with or without cause, subject to the employment laws of the country in which the Employee is employed, subject to any applicable provisions of the corporate law of the country or state in which the Company or the Affiliate is incorporated, as the case may be.

(e) Change in Time Commitment. In the event a Participant's regular level of time commitment in the performance of his or her services for the Company and any Affiliates is reduced (for example, and without limitation, if the Participant is an Employee of the Company and the Employee has a change in status from a full-time Employee to a part-time Employee or takes an extended leave of absence) after the date of grant of any Award to the Participant, the Board has the right in its sole discretion to (x) make a corresponding reduction in the number of shares subject to any portion of such Award that is scheduled to vest or become payable after the date of such change in time commitment, and (y) in lieu of or in combination with such a reduction, extend the vesting or payment schedule applicable to such Award. In the event of any such reduction, the Participant will have no right with respect to any portion of the Award that is so reduced or extended.

(f) Investment Assurances. The Company may require a Participant, as a condition of exercising or acquiring Ordinary Shares under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that the Participant is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Stock Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Ordinary Shares subject to the Stock Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Ordinary Shares. The foregoing requirements, and any assurances given pursuant to such requirements, will be inoperative if (A) the issuance of the shares upon the exercise or acquisition of Ordinary Shares under the Stock Award has been registered under a then currently effective registration statement under the Securities Act, or (B) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on share certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Ordinary Shares.

(g) Withholding Obligations. Unless prohibited by the terms of an Award Agreement, the Company or any Affiliate may, in its sole discretion, but subject always to applicable law, satisfy any federal, state, local or foreign tax withholding obligation, or levies or social security deduction obligation relating to an Award by any of the following means or by a combination of such means: (i) causing the Participant to tender a cash payment; (ii) withholding Ordinary Shares from the Ordinary Shares issued or otherwise issuable to the Participant in connection with the Award; *provided, however,* that no Ordinary Shares are withheld with a value exceeding the maximum amount of tax, levies and social security contribution permitted to be withheld by law or the practice of any revenue authority (or such lesser amount as may be necessary to avoid classification of the Stock Award as a liability for financial accounting purposes); (iii) withholding cash from an Award settled in cash; (iv) withholding payment from any amounts otherwise payable to the Participant; or (v) by such other method as may be set forth in the Award Agreement.

(h) Electronic Delivery. Any reference herein to a "written" agreement or document will include any agreement or document delivered electronically, filed publicly at www.sec.gov (or any successor website thereto) or posted on the Company's intranet (or other shared electronic medium controlled by the Company to which the Participant has access).

(i) Deferrals. To the extent permitted by applicable law, the Board, in its sole discretion, may determine that the delivery of Ordinary Shares or the payment of cash, upon the exercise, vesting or settlement of all or a portion of any Award may be deferred and may establish programs and procedures for deferral elections to be made by Participants. Deferrals by Participants will be made in accordance with Section 409A of the Code. Consistent with Section 409A of the Code, the Board may provide for distributions while a Participant is still an employee or otherwise providing services to the Company or an Affiliate. The Board is authorized to make deferrals of Awards and determine when, and in what annual percentages, Participants may receive payments, including lump sum payments, following the Participant's termination of Continuous Service, and implement such other terms and conditions consistent with the provisions of the Plan and in accordance with applicable law.

(j) Compliance with Section 409A of the Code. To the extent that the Board determines that any Award granted hereunder is subject to Section 409A of the Code, the Award Agreement evidencing such Award shall incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code. To the extent applicable, the Plan and Award Agreements shall be interpreted in accordance with Section 409A of the Code. If required for compliance with Section 409A of the Code, in no event will a Corporate Transaction or a Change in Control, as applicable, be deemed to have occurred if such transaction is not also a "change in the ownership or effective control of" the Company or "a change in the ownership of a substantial portion of the assets of" the Company as determined under Treasury Regulation Section 1.409A-3(i)(5) (without regard to any alternative definition thereunder). Notwithstanding anything to the contrary in the Plan (and unless the Award Agreement specifically provides otherwise), if the Ordinary Shares are publicly traded, and if a Participant holding an Award that constitutes "deferred compensation" under Section 409A of the Code is a "specified employee" for purposes of Section 409A of the Code, no distribution or payment of any amount that is due because of a "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) will be issued or paid before the date that is six months following the date of such Participant's "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) or, if earlier, the date of the Participant's death, unless such distribution or payment can be made in a manner that complies with Section 409A of the Code, and any amounts so deferred will be paid in a lump sum on the day after such six month period elapses, with the balance paid thereafter on the original schedule.

(k) Clawback/Recovery. All Awards granted under the Plan will be subject to recoupment in accordance with any clawback policy that the Company is required to adopt pursuant to the listing standards of any national securities exchange or association on which the Company's securities are listed or as is otherwise required by the U.S. Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law. In addition, the Board may impose such other clawback, recovery or recoupment provisions in an Award Agreement as the Board determines necessary or appropriate, including but not limited to a reacquisition right in respect of previously acquired Ordinary Shares or other cash or property upon the occurrence of an event constituting Cause. No recovery of compensation under such a clawback policy will be an event giving rise to a right to resign for "good reason" or "constructive termination" (or similar term) under any agreement with the Company or an Affiliate.

(l) Securities Compliance. A Participant will not be issued any shares in respect of an Award unless either (i) the shares are 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. Each Award also must comply with other applicable laws and regulations governing the Award, and a Participant will not receive such shares if the Company determines that such receipt would not be in material compliance with such laws and regulations.

(m) Effect on Other Benefit Plans. The value of any Award granted under the Plan, as determined upon grant, vesting or settlement, will not be included as compensation, earnings, salaries, or other similar terms used when calculating any Participant's benefits under any employee benefit plan sponsored by the Company or any Affiliate, except as such plan otherwise expressly provides. The Company expressly reserves its rights to amend, modify, or terminate any of the Company's or any Affiliate's benefit plans.

9. ADJUSTMENTS UPON CHANGES IN ORDINARY SHARES; OTHER CORPORATE EVENTS.

(a) Capitalization Adjustments. In the event of a Capitalization Adjustment, the Board will appropriately and proportionately adjust: (i) the class(es) and maximum number of securities subject to the Plan pursuant to Section 3(a), (ii) the class(es) and maximum number of securities that may be issued pursuant to the exercise of Incentive Stock Options pursuant to Section 3(c), and (iii) the class(es) and number of securities and price per share subject to outstanding Awards. The Board will make such adjustments, and its determination will be final, binding and conclusive; *provided always that* no adjustment may be made which reduces the price payable per Ordinary Share to an amount that is lower than the nominal value of an Ordinary Share.

(b) Dissolution. Except as otherwise provided in the Award Agreement, in the event of a dissolution or liquidation of the Company, all outstanding Stock Awards (other than Stock Awards consisting of vested and outstanding Ordinary Shares not subject to a forfeiture condition or the Company's or any Affiliate's right of repurchase) will terminate immediately prior to the completion of such dissolution or liquidation, and the Ordinary Shares subject to the Company's or any Affiliate's repurchase rights or subject to a forfeiture condition may be repurchased or reacquired by the Company or an Affiliate in accordance with Irish company law notwithstanding the fact that the holder of such Stock Award is providing Continuous Service, *provided, however*, that the Board may, in its sole discretion, cause some or all Stock Awards to become fully vested, exercisable and/or no longer subject to repurchase or forfeiture (to the extent such Stock Awards have not previously expired or terminated) before the dissolution or liquidation is completed but contingent on its completion.

(c) Corporate Transaction. Notwithstanding any other provision of the Plan, the Board may take one or more of the following actions in the event of a Corporate Transaction with respect to Stock Awards, contingent upon the closing or completion of the Corporate Transaction, unless otherwise provided in the instrument evidencing the Stock Award or any other written agreement between the Company or any Affiliate and the Participant or unless otherwise expressly provided by the Board at the time of grant of a Stock Award:

(i) arrange for the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company) to assume or continue the Stock Award or to substitute a similar stock award for the Stock Award (including, but not limited to, an award to acquire the same consideration paid to the shareholders of the Company pursuant to the Corporate Transaction);

(ii) arrange for the assignment of any reacquisition or repurchase rights held by the Company in respect of Ordinary Shares issued pursuant to the Stock Award to the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company);

(iii) accelerate the vesting, in whole or in part, of the Stock Award (and, if applicable, the time at which the Stock Award may be exercised) to a date prior to the effective time of such Corporate Transaction as the Board determines (or, if the Board does not determine such a date, to the date that is five days prior to the effective date of the Corporate Transaction), with such Stock Award terminating if not exercised (if applicable) at or prior to the effective time of the Corporate Transaction; provided, however, that the Board may require Participants to complete and deliver to the Company a notice of exercise before the effective date of a Corporate Transaction, which exercise is contingent upon the effectiveness of such Corporate Transaction; *provided, however*, that the Board may require Participants to complete and deliver to the Company a notice of exercise before the effective date of a Corporate Transaction;

(iv) arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by the Company with respect to the Stock Award;

(v) cancel or arrange for the cancellation of the Stock Award, to the extent not vested or not exercised prior to the effective time of the Corporate Transaction, in exchange for no consideration (U.S. $0) or such cash consideration, if any, as the Board, in its sole discretion, may consider appropriate; and

(vi) cancel or arrange for the cancellation of the Stock Award, to the extent not exercised prior to the effective time of the Corporate Transaction, in exchange for a payment, in such form as may be determined by the Board equal to the excess, if any, of (A) the per share amount (or value of property per share) payable to holders of Ordinary Shares in connection with the Corporate Transaction, over (B) the per share exercise price under the applicable Stock Award, multiplied by the number of vested shares subject to the Stock Award. For clarity, this payment may be zero (U.S. $0) if the amount per share (or value of property per share) payable to the holders of Ordinary Shares is equal to or less than the per share exercise price of the Stock Award. In addition, any escrow, holdback, earnout or similar provisions in the definitive agreement for the Corporate Transaction may apply to such payment to the holder of the Stock Award to the same extent and in the same manner as such provisions apply generally to the holders of Ordinary Shares.

The Board need not take the same action or actions with respect to all Stock Awards or portions thereof or with respect to all Participants. The Board may take different actions with respect to the vested and unvested portions of a Stock Award.

(d) Acceleration on a Qualifying Termination in Connection with a Change in Control . If during the period beginning on the date that is 30 days prior to and ending on the date that is 12 months following the consummation of a Corporate Transaction that also qualifies as a Change in Control, (i) a Participant's services to the Company (or its successor in the Change in Control) in all capacities are involuntarily terminated without Cause, or (ii) a Participant resigns service to the Company (or its successor in the Change in Control) in all capacities for Good Reason, and in either case other than as a result of death or Disability, then as of the date of Participant's termination of Continuous Service, the vesting and exercisability of any then-unvested Stock Award held by a Participant shall be accelerated in full.

10. AMENDMENT, TERMINATION SUSPENSION OF THE PLAN OR ADOPTION OF SUB-PLANS.

(a) Plan Term. The Board may suspend or terminate the Plan at any time. No Incentive Stock Options may be granted after the tenth anniversary of the earlier of (i) the Adoption Date, or (ii) the date the Plan is approved by the shareholders of the Company No Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) Amendments. To amend the Plan in any respect the Board deems necessary or advisable. However, except as provided in Section 9(a) relating to Capitalization Adjustments, to the extent required by applicable law or listing requirements, shareholder approval shall be required for any amendment of the Plan that either (A) materially increases the number of Ordinary Shares available for issuance under the Plan, (B) materially expands the class of individuals eligible to receive Awards under the Plan, (C) materially increases the benefits accruing to Participants under the Plan or materially reduces the price at which Ordinary Shares may be issued or purchased under the Plan, (D) materially extends the term of the Plan, or (E) expands the types of Awards available for issuance under the Plan. Except as provided above, rights under any Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (1) the Company requests the consent of the affected Participant, and (2) such Participant consents in writing.

(c) No Impairment of Rights. Amendment, suspension or termination of the Plan will not materially impair rights and obligations under any Award granted while the Plan is in effect except with the written consent of the affected Participant or as otherwise permitted in the Plan.

(d) Sub-Plans. The Board shall be entitled to adopt sub-plans to the Plan pursuant to which Awards may be made on such terms and conditions different from those specified in the Plan as may, in the judgment of the Board, be necessary or desirable in order to recognize differences in local law, tax policy or practices, subject to any required shareholder approval as contemplated in Section 9(b).

11. EFFECTIVE DATE OF PLAN.

The Plan will come into existence on the Adoption Date (the "***Effective Date***"); *provided, however*, no Award may be granted prior to the IPO Date. In addition, no Stock Award may be exercised (or, in the case of a Restricted Stock Award, Restricted Stock Unit Award, Performance Stock Award, or Other Stock Award, may be granted), unless and until the Plan has been approved by the shareholders of the Company, which approval will be within 12 months after the Adoption Date.

12. CHOICE OF LAW.

This Plan shall 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.

13. DEFINITIONS. As used in the Plan, the following definitions will apply to the capitalized terms indicated below:

(a) "***Adoption Date***" means the date the Plan is adopted by the Board.

(b) "***Affiliate***" means, at the time of determination, any "parent" or "majority-owned subsidiary" of the Company, as such terms are defined in Rule 405 of the Securities Act or, as the context so requires, means a "holding company" or "subsidiary" of the Company as such terms are defined in Irish company law. The Board will have the authority to determine the time or times at which "parent" or "subsidiary" status is determined within the foregoing definition.

(c) "***Award***" means a Stock Award or a Performance Cash Award.

(d) "***Award Agreement***" means a written agreement between the Company and a Participant evidencing the terms and conditions of an Award.

(e) "***Board***" means the Board of Directors of the Company.

(f) "***Capitalization Adjustment***" means any change that is made in, or other events that occur with respect to, the Ordinary Shares subject to the Plan or subject to any Stock Award after the Effective Date without the receipt of consideration by the Company through merger, consolidation, reorganization, recapitalization, reincorporation, share dividend, dividend in property other than cash, large nonrecurring cash dividend, share split or reverse share split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure, or any similar equity restructuring transaction, as that term is used in Statement of Financial Accounting Standards Board Accounting Standards Codification Topic 718 (or any successor thereto). Notwithstanding the foregoing, the conversion of any convertible securities of the Company will not be treated as a Capitalization Adjustment.

(g) "***Cause***" will have the meaning ascribed to such term in any written agreement between the Participant and the Company defining such term and, in the absence of such agreement, such term means, with respect to a Participant, the occurrence of any of the following events: (i) such Participant's commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof or any country in which a Participant is employed; (ii) such Participant's attempted commission of, or participation in, a fraud or act of dishonesty against the Company or an Affiliate; (iii) such Participant's intentional, material violation of any contract or agreement between the Participant and the Company or an Affiliate, of any statutory duty owed to the Company or an Affiliate; (iv) such Participant's unauthorized use or disclosure of the confidential information or trade secrets of the Company or an Affiliate; or (v) such Participant's gross misconduct. The determination that a termination of the Participant's Continuous Service is either for Cause or without Cause will be made by the Company, in its sole discretion. Any determination by the Company that the Continuous Service of a Participant was terminated with or without Cause for the purposes of outstanding Stock Awards held by such Participant will have no effect upon any determination of the rights or obligations of the Company or an Affiliate or such Participant for any other purpose.

(h) "***Change in Control***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) any Exchange Act Person becomes the Owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities other than by virtue of a merger, consolidation or similar transaction. Notwithstanding the foregoing, a Change in Control shall not be deemed to occur (A) on account of the acquisition of securities of the Company directly from the Company, (B) on account of the acquisition of securities of the Company by an investor, any affiliate thereof or any other Exchange Act Person that acquires the Company's securities in a transaction or series of related transactions the primary purpose of which is to obtain financing for the Company through the issuance of equity securities, or (C) solely because the level of Ownership held by any Exchange Act Person (the "***Subject Person***") exceeds the designated percentage threshold of the outstanding voting securities as a result of a repurchase or other acquisition of voting securities by the Company or any Affiliate reducing the number of shares outstanding, provided that if a Change in Control would occur (but for the operation of this sentence) as a result of the acquisition of voting securities by the Company or any Affiliate, and after such share acquisition, the Subject Person becomes the Owner of any additional voting securities that, assuming the repurchase or other acquisition had not occurred, increases the percentage of the then outstanding voting securities Owned by the Subject Person over the designated percentage threshold, then a Change in Control shall be deemed to occur;

(ii) a merger, consolidation or similar transaction involving (directly or indirectly) the Company and, immediately after the consummation of such merger, consolidation or similar transaction, the shareholders of the Company immediately prior thereto do not Own, directly or indirectly, either (A) outstanding voting securities representing more than 50% of the combined outstanding voting power of the surviving Entity in such merger, consolidation or similar transaction or (B) more than 50% of the combined outstanding voting power of the parent of the surviving Entity in such merger, consolidation or similar transaction, in each case in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such transaction;

(iii) the shareholders of the Company approve or the Board approves a plan of complete dissolution or liquidation of the Company, or a complete dissolution or liquidation of the Company shall otherwise occur, except for a liquidation into a parent corporation;

(iv) a sale, lease, exclusive license or other disposition of all or substantially all (as determined by the Board in its sole discretion) of the consolidated assets of the Company and its Subsidiaries, other than a sale, lease, license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries to an Entity, more than 50% of the combined voting power of the voting securities of which are Owned by shareholders of the Company in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such sale, lease, license or other disposition; or

(v) individuals who, on the date the Plan is adopted by the Board, are members of the Board (the "***Incumbent Board***") cease for any reason to constitute at least a majority of the members of the Board; *provided, however*, that if the appointment or election (or nomination for election) of any new Board member was approved or recommended by a majority vote of the members of the Incumbent Board then still in office, such new member shall, for purposes of this Plan, be considered as a member of the Incumbent Board.

For the avoidance of doubt, any one or more of the above events may be effected pursuant to (i) a compromise or arrangement sanctioned by the Irish courts under section 450 of the Irish Companies Act 2014 (as may be amended, updated or replaced from time to time) (the "***2014 Act***") or (ii) a scheme, contract or offer which has become binding on all shareholders pursuant to Section 609 of the 2014 Act, or (iii) a bid pursuant to Regulation 23 or 24 of the European Communities (Takeover Bids (Directive 2004/25/EC)) Regulations 2006.

Notwithstanding the foregoing or any other provision of this Plan, (A) the term Change in Control shall not include a sale of assets, merger or other transaction effected exclusively for the purpose of changing the domicile of the Company, and (B) the definition of Change in Control (or any analogous term) in an individual written agreement between the Company or any Affiliate and the Participant shall supersede the foregoing definition with respect to Awards subject to such agreement; *provided, however*, that if no definition of Change in Control or any analogous term is set forth in such an individual written agreement, the foregoing definition shall apply.

(i) "***Code***" means the U.S. Internal Revenue Code of 1986, as amended, including any applicable regulations and guidance thereunder.

(j) "***Committee***" means a committee of one or more Directors to whom authority has been delegated by the Board in accordance with Section 2(c).

(k) "***Company***" means Iterum Therapeutics Public Limited Company, a company incorporated under the laws of the Republic of Ireland.

(l) "***Continuous Service***" means that the Participant's service with the Company or an Affiliate, whether as an Employee or Director is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee or Director or a change in the Entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, will not terminate a Participant's Continuous Service; *provided, however,* that if the Entity for which a Participant is rendering services ceases to qualify as an Affiliate, as determined by the Board in its sole discretion, such Participant's Continuous Service will be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. To the extent permitted by law, the Board, the chief executive officer of the Company (or an Affiliate, if applicable) or the Stock Plan Administrator, in that party's sole discretion, may determine whether Continuous Service will be considered interrupted in the case of (i) any leave of absence approved by the Company (or an Affiliate, if applicable), including sick leave, military leave or any other personal leave, or (ii) transfers between the Company, an Affiliate, or their successors. Notwithstanding the foregoing, a leave of absence will be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company's (or an Affiliate's, if applicable) leave of absence policy, in the written terms of any leave of absence agreement or policy applicable to the Participant, or as otherwise required by law.

(m) "***Corporate Transaction***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) a sale or other disposition of all or substantially all, as determined by the Board, in its sole discretion, of the consolidated assets of the Company and its Subsidiaries;

(ii) a sale or other disposition of at least 50% of the outstanding securities of the Company;

(iii) a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or

(iv) a merger, consolidation or similar transaction following which the Company is the surviving corporation but the Ordinary Shares outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

For the avoidance of doubt, 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 2014 Act or (z) Chapter 2 of Part 9 of the 2014 Act.

(n) "***Director***" means a member of the Board.

(o) "***Disability***" means, with respect to a Participant, the inability of such Participant to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or that has lasted or can be expected to last for a continuous period of not less than twelve (12) months as provided in Sections 22(e)(3) and 409A(a)(2)(c)(i) of the Code, and will be determined by the Board on the basis of such medical evidence as the Board deems warranted under the circumstances.

(p) "***Employee***" means any person employed by the Company or an Affiliate.

(q) "***Entity***" means a corporation, partnership, limited liability company or other entity.

(r) "***Exchange Act***" means the U.S. Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

(s) "***Exchange Act Person***" means any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that "Exchange Act Person" shall not include (i) the Company or any Subsidiary of the Company, (ii) any employee benefit plan of the Company or any Subsidiary of the Company or any trustee or other fiduciary holding securities under an employee benefit plan of the Company or any Subsidiary of the Company, (iii) an underwriter temporarily holding securities pursuant to a registered public offering of such securities, (iv) an Entity Owned, directly or indirectly, by the shareholders of the Company in substantially the same proportions as their Ownership of Ordinary Shares of the Company; or (v) any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act) that, as of the Effective Date, is the Owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities.

(t) "***Fair Market Value***" means, as of any date, the value of the Ordinary Shares determined as follows:

(i) If the Ordinary Shares is listed on any established stock exchange or traded on the NASDAQ Global Market or the NASDAQ Global Select Market, the Fair Market Value of a share of Ordinary Shares, unless otherwise determined by the Board, shall be the closing sales price for such Ordinary Shares as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Ordinary Shares) on the day of determination, as reported in a source the Board deems reliable.

(ii) Unless otherwise provided by the Board, if there is no closing sales price for the Ordinary Shares on the day of determination, then the Fair Market Value shall be the closing selling price on the last preceding date for which such quotation exists.

(iii) In the absence of such markets for the Ordinary Shares, the Fair Market Value shall be determined by the Board in good faith and in a manner that complies with Sections 409A and 422 of the Code.

(a) "***Good Reason***" will have the meaning ascribed to such term in any written agreement between the Participant and the Company or a successor corporation defining such term and, in the absence of such agreement, such term means, with respect to a Participant, any of the following actions taken without Cause without Participant's consent:

(i) A material reduction of the Participant's base compensation, other than a reduction that applies generally to all executives;

(i) A material reduction in the Participant's authority, duties or responsibilities, provided, however, that a change in job position (including a change in title) shall not be deemed a "material reduction" unless the Participant's new authority, duties or responsibilities are materially reduced from the prior authority, duties or responsibilities;

(i) failure or refusal of a successor to the Company to materially assume the Company's obligations under the Participant's offer letter and/or employment agreement, if applicable, in the event of a Change in Control; or

(i) relocation of the Participant's principal place of employment that results in an increase in the Participant's one-way driving distance by more than 50 miles from the Participant's then current principal residence.

In order to resign for Good Reason, the Participant must provide written notice of the event giving rise to Good Reason to the Company within 90 days after the condition arises, allow the Company at least 30 days to cure such condition, and if the Company fails to cure the condition within such period, then Participant's resignation from all positions the Participant then holds with the Company must be effective not later than 90 days after the end of the Company's cure period.

(u) "***Incentive Stock Option***" means an option granted pursuant to Section 5 of the Plan that is intended to be, and that qualifies as, an "incentive stock option" within the meaning of Section 422 of the Code.

(v) "***IPO Date***" means the date of the underwriting agreement between the Company and the underwriter(s) managing the initial public offering of the Ordinary Shares, pursuant to which the Ordinary Shares are priced for the initial public offering.

(w) "***Non-Employee Director***" means a Director who either (i) is not a current employee or officer of the Company or an Affiliate, does not receive compensation, either directly or indirectly, from the Company or an Affiliate for services rendered as a consultant or in any capacity other than as a Director (except for an amount as to which disclosure would not be required under Item 404(a) of Regulation S-K promulgated pursuant to the Securities Act ("***Regulation S-K***")), does not possess an interest in any other transaction for which disclosure would be required under Item 404(a) of Regulation S-K, and is not engaged in a business relationship for which disclosure would be required pursuant to Item 404(b) of Regulation S-K; or (ii) is otherwise considered a "non-employee director" for purposes of Rule 16b-3.

(x) "***Nonstatutory Stock Option***" means an option granted pursuant to Section 5 of the Plan that does not qualify as an Incentive Stock Option.

(y) "***Officer***" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act.

(z) "***Option***" means an Incentive Stock Option or a Nonstatutory Stock Option to purchase Ordinary Shares granted pursuant to the Plan.

(aa) "***Ordinary Shares***" or "***Shares***" means the Ordinary Shares in the capital of the Company.

(bb) "***Other Stock Award***" means an award based in whole or in part by reference to the Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(d).

(cc) "***Own,***" "***Owned,***" "***Owner,***" "***Ownership***" A person or Entity shall be deemed to "Own," to have "Owned," to be the "Owner" of, or to have acquired "Ownership" of securities if such person or Entity, directly or indirectly, through any contract, arrangement, understanding, relationship or otherwise, has or shares voting power, which includes the power to vote or to direct the voting, with respect to such securities.

(dd) "***Participant***" means a person to whom an Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Stock Award.

(ee) "***Performance Cash Award***" means an award of cash granted pursuant to the terms and conditions of Section 6(c)(ii).

(ff) "***Performance Criteria***" means one or more criteria that the Board will select for purposes of establishing the Performance Goals for a Performance Period. The Performance Criteria that will be used to establish such Performance Goals may be based on any one of, or combination of, the following as determined by the Board: (1) earnings (including earnings per share and net earnings); (2) earnings before interest, taxes and depreciation; (3) earnings before interest, taxes, depreciation and amortization; (4) earnings before interest, taxes, depreciation, amortization and legal settlements; (5) earnings before interest, taxes, depreciation, amortization, legal settlements and other income (expense); (6) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense) and stock-based compensation; (7) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense), stock-based compensation and changes in deferred revenue; (8) total stockholder return; (9) return on equity or average stockholder's equity; (10) return on assets, investment, or capital employed; (11) stock price; (12) margin (including gross margin); (13) income (before or after taxes); (14) operating income; (15) operating income after taxes; (16) pre-tax profit; (17) operating cash flow; (18) sales or revenue targets; (19) increases in revenue or product revenue; (20) expenses and cost reduction goals; (21) improvement in or attainment of working capital levels; (22) economic value added (or an equivalent metric); (23) market share; (24) cash flow; (25) cash flow per share; (26) share price performance; (27) debt reduction; (28) implementation or completion of projects or processes (including, without limitation, clinical trial initiation, clinical trial enrollment, clinical trial results, new and supplemental indications for existing products, regulatory filing submissions, regulatory filing acceptances, regulatory or advisory committee interactions, regulatory approvals, and product supply); (29) stockholders' equity; (30) capital expenditures; (31) debt levels; (32) operating profit or net operating profit; (33) workforce diversity; (34) growth of net income or operating income; (35) billings; (36) bookings; (37) employee retention; (38) initiation of phases of clinical trials and/or studies by specific dates; (39) patient enrollment rates; (40) budget management; (41) submission to, or approval by, a regulatory body (including, but not limited to the U.S. Food and Drug Administration) of an applicable filing or a product candidate; (42) regulatory milestones; (43) progress of internal research or clinical programs; (44) progress of partnered programs; (45) partner satisfaction; (46) timely completion of clinical trials; (47) submission of INDs and NDAs and other regulatory achievements; (48) research progress, including the development of programs; (49) strategic partnerships or transactions (including in-licensing and out-licensing of intellectual property; (50) customer satisfaction; and (51) other measures of performance selected by the Board.

(gg) "***Performance Goals***" means, one or more goals established by the Board for the Performance Period based upon the Performance Criteria. Performance Goals may be based on a Company-wide basis, with respect to one or more business units, divisions, Affiliates, or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Unless specified otherwise by the Board (i) in the Award Agreement at the time the Award is granted or (ii) in such other document setting forth the Performance Goals at the time the Performance Goals are established, the Board will appropriately make adjustments in the method of calculating the attainment of Performance Goals for a Performance Period as follows: (1) to exclude restructuring and/or other nonrecurring charges; (2) to exclude exchange rate effects; (3) to exclude the effects of changes to generally accepted accounting principles; (4) to exclude the effects of any statutory adjustments to corporate tax rates; (5) to exclude the effects of any items that are unusual in nature or occur infrequently as determined under generally accepted accounting principles; (6) to exclude the dilutive effects of acquisitions or joint ventures; (7) to assume that any business divested by the Company achieved performance objectives at targeted levels during the balance of a Performance Period following such divestiture; (8) to exclude the effect of any change in the

outstanding shares of common stock of the Company by reason of any stock dividend or split, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common stockholders other than regular cash dividends; (9) to exclude the effects of stock based compensation and the award of bonuses under the Company's bonus plans; (10) to exclude costs incurred in connection with potential acquisitions or divestitures that are required to be expensed under generally accepted accounting principles; (11) to exclude the goodwill and intangible asset impairment charges that are required to be recorded under generally accepted accounting principles; and (12) to exclude the effect of any other unusual, non-recurring gain or loss or other extraordinary item. In addition, the Board retains the discretion to reduce or eliminate the compensation or economic benefit due upon attainment of Performance Goals and to define the manner of calculating the Performance Criteria it selects to use for such Performance Period. Partial achievement of the specified criteria may result in the payment or vesting corresponding to the degree of achievement as specified in the Award Agreement or the written terms of a Performance Cash Award.

(hh) "***Performance Period***" means the period of time selected by the Board over which the attainment of one or more Performance Goals will be measured for the purpose of determining a Participant's right to and the payment of a Stock Award or a Performance Cash Award. Performance Periods may be of varying and overlapping duration, at the sole discretion of the Board.

(ii) "***Performance Stock Award***" means a Stock Award granted under the terms and conditions of Section 6(c)(i).

(jj) ***"Personal Data"*** has the same meaning as defined in the Data Protection Acts 1988 and 2003.

(kk) "***Plan***" means this Iterum Therapeutics Public Limited Company 2018 Equity Incentive Plan.

(ll) "***Restricted Stock Award***" means an award of Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(a).

(mm) "***Restricted Stock Unit Award***" means a right to receive Ordinary Shares which is granted pursuant to the terms and conditions of Section 6(b).

(nn) "***Rule 16b-3***" means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.

(oo) "***Securities Act***" means the U.S. Securities Act of 1933, as amended.

(pp) "***Stock Appreciation Right***" or "***SAR***" means a right to receive the appreciation on Ordinary Shares that is granted pursuant to the terms and conditions of Section 5.

(qq) "***Stock Award***" means any right to receive Ordinary Shares granted under the Plan, including an Incentive Stock Option, a Nonstatutory Stock Option, a Restricted Stock Award, a Restricted Stock Unit Award, a Stock Appreciation Right, a Performance Stock Award or any Other Stock Award.

(rr) "***Stock Plan Administrator***" means one or more Officers or Employees designated by the Board pursuant to Section 2(a).

(ss) "***Subsidiary***" means, with respect to the Company, (i) any corporation of which more than 50% of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors of such corporation (irrespective of whether, at the time, stock of any other class or classes of such corporation will have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, Owned by the Company, and (ii) any partnership, limited liability company or other entity in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than 50%, or, where the context so requires, the definition of "subsidiary" in Irish company law.

(tt) "***Ten Percent Shareholder***" means a person who Owns (or is deemed to Own pursuant to Section 424(d) of the Code) shares possessing more than 10% of the total combined voting power of all classes of shares of the Company or any Affiliate.

PLAN ADOPTION AND AMENDMENTS

Adopted by the Board of Directors of Iterum Therapeutics Public Limited Company on 14 March, 2018.

Approved by the shareholders of Iterum Therapeutics Public Limited Company on [__], 2018.

ITERUM THERAPEUTICS PUBLIC LIMITED COMPANY

2018 EQUITY INCENTIVE PLAN – SUB PLAN FOR NON-EMPLOYEE DIRECTORS AND CONSULTANTS

1 **ESTABLISHMENT AND PURPOSE**

This sub-plan is established by the Board in accordance with Section 10(d) of the Iterum Therapeutics Public Limited Company 2018 Incentive Plan (the "**Plan"**) for the purposes of granting Awards to Non—Employee Directors and Consultants of Iterum Therapeutics Public Limited Company and its Subsidiaries. This sub-plan shall be known as the "**NED and Consultant Sub-Plan**" or "**Sub-Plan**".

2 **RULES**

2.1 The provisions of the Plan shall apply in their entirety to Awards made under this Sub-Plan save and expect only as set out in Sections 3 and 4 below. Capitalized terms contained in this Sub-Plan that are not defined herein shall have the same meanings given to them in the Plan.

2.2 The terms of this Sub-Plan shall also apply to Awards originally granted under the Plan to Employees, if such individual subsequently experiences a change in status from an Employee to either a Consultant or a Non-Employee Director without a break in Continuous Service.

2.3 For clarity, any Awards granted under this Sub-Plan will be deemed to be granted from the Plan for purposes of reducing the number of shares available under the Share Reserve. Shares subject to Awards that are forfeited, cancelled or expire in the manner contemplated by Section 3(b) of the Plan will be added back to the Share Reserve as provided therein.

3 **DEFINITIONS**

3.1 The following definition shall be inserted for the purposes of this Sub-Plan:

Consultant means any person, including an advisor, who is (i) engaged by the Company or an Affiliate to render consulting or advisory services and is compensated for such services, or (ii) serving as a member of the board of directors of an Affiliate and is compensated for such services. However, service solely as a Non-Employee Director, or payment of a fee for such service, will not cause a Non-Employee Director to be considered a "Consultant" for purposes of the Plan. Notwithstanding the foregoing, a person is treated as a Consultant under this Plan only if a Form S-8 Registration Statement under the Securities Act is available to register either the offer or the sale of the Company's securities to such person;

3.2 The following definitions shall be deleted and replaced with the following for the purposes if this Sub-Plan:

Continuous Service means that the Participant's service with the Company or an Affiliate, whether as a Director or Consultant, is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as Director or Consultant or a change in the Entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, will not terminate a Participant's Continuous Service; provided, however, that if the Entity for which a Participant is rendering services ceases to qualify as an Affiliate, as determined by the Board in its sole discretion, such Participant's Continuous Service will be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. To the extent permitted by law, the Board, the chief executive officer of the Company (or an Affiliate, if applicable) or the Stock Plan Administrator, in that party's sole discretion, may determine whether Continuous Service will be considered interrupted in the case of (i) any interruption of service approved by the Company (or an Affiliate, if applicable), including sick leave, interruption of service or any other personal leave, or (ii) transfers of service between the Company, an Affiliate, or their successors. Notwithstanding the foregoing, a leave of absence will be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company's (or an Affiliate's, if applicable) leave of absence policy, in the written terms of any agreement or policy applicable to the Participant, or as otherwise required by law;

Good Reason will have the meaning ascribed to such term in any written agreement between the Participant and the Company or a successor corporation defining such term and, in the absence of such agreement, such term means, with respect to a Participant, any of the following actions taken without Cause without Participant's consent:

(i) a material reduction of the Participant's base service fee, other than a reduction that applies generally to all Non-Employee Directors or Consultants;

(ii) a material reduction in the Participant's authority, duties or responsibilities; or

(iii) failure or refusal of a successor to the Company to materially assume the Company's obligations under the Participant's service agreement, if applicable, in the event of a Change in Control;

In order to terminate service for Good Reason, the Participant must provide written notice of the event giving rise to Good Reason to the Company within 90 days after the condition arises, allow the Company at least 30 days to cure such condition, and if the Company fails to cure the condition within such period, then Participant's termination of service must be effective not later than 90 days after the end of the Company's cure period; and

4 **SECTIONS**

In this Sub-Plan:

4.1 Section 1(b) of the Plan shall be deleted and replaced with the following:

1(b)—Eligible Awards Recipients. The person eligible to receive Awards are Non-Employee Directors and Consultants.

4.2 Section 2(d) shall be deleted and replaced with the following:

2(d) – Delegation to an Officer. Subject to compliance with Irish law, the Board may delegate to one of more Officers the authority to do one or both of the following: (i) designate Non-Employee Directors and Consultants who are providing Continuous Service to the Company or any of its Subsidiaries to be recipients of Stock Awards and the terms thereof, and (ii) determine the number of Ordinary Shares to be subject to Board resolutions regarding such delegation shall specify the total number of Ordinary Shares that may be subject to the Stock Awards granted by such Officer and that such Officer many not grant a Stock Awards to himself or herself. Notwithstanding the foregoing, the Board may not delegate authority to an Officer to determine the fair Market Value of the Ordinary Shares.

4.3 Section 3(b) of the Plan shall be deleted and replaced with the following:

3(b)—Reversion of Shares to the Share Reserve. If subject to compliance with Irish law (i) any Ordinary Shares issued pursuant to a Stock Award are forfeited back to or repurchased by the Company or any Affiliate because of the failure to meet a contingency or condition required for the vesting of such Ordinary Shares, or (ii) any Ordinary Shares are cancelled in accordance with the cancellation and regrant provisions of Section 2(b)(x), then the Ordinary Shares that are forfeited, repurchased or cancelled shall revert to and again become available for issuance under the Plan. If any Ordinary Shares subject to a Stock Award are not delivered to a Participant because an appreciation distribution in respect of a Stock Appreciation Right is paid in Ordinary Shares, the number of Ordinary Shares subject to the Stock Award that are not delivered to the Participant shall remain available for subsequent issuance under the Plan.

4.4 Section 5(c) of the Plan shall be deleted and replaced with the following:

5(c)—Exercise and Purchase Price for Options. To exercise any outstanding Option, the Participant must provide written notice of exercise to the Company in the manner determined by the Stock Plan Administrator. The purchase price of Ordinary Shares acquired pursuant to the exercise of an Option may be paid, to the extent permitted by applicable law and as determined by the Board in its sole discretion, by any combination of the methods of payment set forth below. The Board will have the authority to grant Options that do not permit all of the following methods of payment (or otherwise restrict the ability to use certain methods) and to grant Options that require the consent of the Company to use a particular method of payment. In all cases the Company shall require that the nominal value of each newly issued Ordinary Share is fully paid up. The permitted methods of payment are as follows:

(i) by cash, check, bank draft or money order payable to the Company;

(ii) pursuant to a program developed under Regulation T as promulgated by the U.S. Federal Reserve Board that, prior to the issuance of Ordinary Shares subject to the Option, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds;

(iii) deduction from service fees due and payable to aNon-Employee Director or Consultant by the Company or any Affiliate; or

(iv) in any other form of legal consideration that may be acceptable to the Board or the Stock Plan Administration and permissible under applicable law.

4.5 Section 8(d) shall be deleted and replaces with the following:

8(d) – No Service Rights. Nothing in the Plan, any Award Agreement or any other instrument executed thereunder or in connection with any Award granted pursuant thereto will confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Award was granted or will affect any right that the Company or an Affiliate may have to terminate (i) the service of a Director pursuant to the Constitution of the Company or an Affiliate, or (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or and Affiliate, or any applicable provisions of the corporate law of the country or state in which the Company or the Affiliate is incorporated as the case may be.

4.6 Rule 8 (g) of the Plan shall be deleted and replaced with the following:

8(g)—Withholding Obligations. Unless prohibited by the terms of an Award Agreement, the Company or any Affiliate may, in its sole discretion, but subject always to applicable law, satisfy any federal, state, local or foreign tax withholding obligation, or levies or social security deduction obligation relating to an Award by any of the following means or by a combination of such means: (i) causing the Participant to tender a cash payment; (ii) implementing a sell-to cover arrangement (iii) withholding cash from an Award settled in cash; (iv) withholding payment from any amounts otherwise payable to the Participant; or (v) by such other method as may be set forth in the Award Agreement subject to compliance with applicable law.

ITERUM THERAPEUTICS PLC
NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

Members of the board of directors (the "***Board***") of Iterum Therapeutics plc (the "***Company***") shall be eligible to receive the cash and equity compensation for their service on the Board and any committee of the Board (a "***Committee***") as set forth in this Non-Employee Director Compensation Policy (this "***Policy***"). The cash compensation and equity grants described in this Policy shall be paid or be made, as applicable, to each member of the Board who is not an employee of the Company or any parent or subsidiary of the Company (each, a "***Director***"), unless such Director declines the receipt of such cash compensation or equity grants by written notice to the Company. No separate compensation for Board service shall be paid to any member of the Board who is an employee of the Company or any parent or subsidiary of the Company. This Policy shall remain in effect until it is amended or rescinded by further action of the Board.

Cash Compensation

Commencing upon the execution and delivery of the underwriting agreement between the Company and the underwriters managing the Company's initial public offering (the "***IPO Date***"), each Director shall be eligible to receive the annual cash retainers described below. The annual cash retainers will be paid in four equal quarterly installments in arrears, and will be fully vested and earned when paid.

Each Director shall be eligible to receive an annual cash retainer of $35,000 for service on the Board. The non-executive chairperson of the Board shall be eligible to receive an additional annual cash retainer of $27,500 for such service.

In addition, the Directors shall be eligible to receive annual cash retainers for service on our Committees as follows:

- The chairperson of the Audit Committee shall be eligible to receive an annual cash retainer of $15,000 for such service, and each of the other members of the Audit Committee shall be eligible to receive an annual cash retainer of $7,500.
- The chairperson of the Compensation Committee shall be eligible to receive an annual cash retainer of $12,000 for such service, and each of the other members of the Compensation Committee shall be eligible to receive an annual cash retainer of $6,000.
- The chairperson of the Nominating and Corporate Governance Committee shall be eligible to receive an annual cash retainer of $8,000 for such service, and each of the other members of the Nominating and Corporate Governance Committee shall be eligible to receive an annual cash retainer of $4,000.

The first installment of the cash retainers described above following the IPO date will be prorated for the number of actual days remaining in such calendar quarter. In addition, each person who is elected or appointed to be a Director or who is appointed to serve as non-executive chairperson of the Board or a member or chairperson of one of the Committees described above, in each case other than on the first day of a calendar quarter, shall be eligible to receive a pro rata amount of the annual cash retainers described above with respect to the calendar quarter in which such person becomes a Director, non-executive chairperson or a member or chairperson of one of the Committees, as applicable, which pro rata amount reflects a reduction for each day during the calendar quarter prior to the date of such election or appointment.

Equity Compensation

General Terms. The equity compensation set forth below will be granted under the Iterum Therapeutics Public Limited Company Equity Incentive Plan—Sub Plan for Non-Employee Directors and Consultants, as may be amended from time to time (the "***Plan***"). Each stock option and restricted stock unit award, as applicable, will be subject to the terms and conditions in the forms of award agreements previously approved by the Board or the Compensation Committee, as applicable, for use in connection with grants to Directors under this Policy.

All stock options granted under this Policy will be nonstatutory stock options, with an exercise price per share equal to 100% of the Fair Market Value (as defined in the Plan) of the underlying Company ordinary shares on the date of grant (provided, that in all cases, the exercise price shall not be less than the nominal value of the Company's ordinary shares), and a term of ten (10) years from the date of grant (subject to earlier termination in connection with a termination of service as provided in the Plan). Stock options will be "early exercisable," and each Director will timely provide to the Company a copy of any election made under Section 83(b) of the U.S. Internal Revenue Code, as amended (or similar election under non-U.S. tax laws), if applicable.

Annual Equity Grant. At the close of business on the date of each annual shareholder meeting of the Company, each Director will be automatically, and without further action by the Board, receive annual equity awards (collectively referred to as the "***Annual Equity Grant***") as follows:

- Each director shall receive an Annual Equity Grant determined in accordance with the rules below based on an aggregate grant date value of US$80,000.
- The Annual Equity Grant shall be granted as a mix of options and restricted stock units, at each individual Director's election. Each Director must determine his or her mix of equity awards through written election (in the manner designated by the Company) no later than 30 days prior to the applicable grant date for the Annual Equity Grant. In the event that a Director fails to make an election by the deadline, such Director's Annual Equity Grant will automatically be granted as (i) a stock option with a grant date value of US$40,000 and (ii) a restricted stock unit award with a grant date value of US$40,000.
- Each stock option will vest in full upon the first anniversary of the date of grant, and each restricted stock unit award will vest in full upon the first anniversary of the date of grant, in each case subject to the Director's Continuous Service (as defined in the Plan) through each applicable vesting date.
- The actual number of shares under a stock option to be granted under this Policy will be determined using the same method the Company uses to calculate the grant-date fair value of stock options in its financial statements, except that no provision will be made for estimated forfeitures related to service-based vesting. The actual number of shares under a restricted stock unit award to be granted 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).
- If a Director is first elected or appointed to the Board following the date of the annual shareholder meeting of the Company, such Director will receive a prorated Annual Equity Grant with the number of shares underlying such grant determined based on the number of days between the date such Director joins the Board and the calendar day of the prior annual shareholder meeting. For example, if the annual shareholder meeting was held on May 1, 2019 and a new Director

joins the Board on September 2, 2019, the number of shares under the Annual Equity Grant will be prorated assuming that the next annual shareholder meeting were held on May 1, 2020 (regardless of the day such meeting is actually held).

IPO Grant. On the IPO Date, each Director will automatically, and without further action by the Board, receive an equity grant representing the same grant date value and determined in accordance with the rules as provided above with respect to the Annual Equity Grant (the "***IPO Grant***").

Expense Reimbursements

The Company will reimburse each Director for his or her reasonable travel (including airfare and ground transportation), lodging and meal expenses incidental to in-person attendance at and participation in in Board and/or Committee meetings, provided that such Director timely submit to the Company appropriate documentation substantiating such expenses.

If any expense reimbursement payment is subject to tax imposed by the Irish Revenue Commissioners ("***Revenue***"), each Director will also be entitled to a payment, up to an amount ("***Gross-Up Payment***") such that after the deduction of all taxes (including, without limitation, any income taxes calculated at the rate applicable to each Director for the year in which the expenses were incurred) on the Gross-Up Payment, the Director will retain an amount equal to the full reimbursement payment. Such Gross-Up Payment be made no later than the last day of such individual's taxable year that immediately follows the taxable year in which the taxable expense was incurred. All taxes due will be paid by the Company to Revenue.

* * * * * * *

Adopted by the Board of Directors of Iterum Therapeutics plc on [ ] May 2018.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Iterum Therapeutics plc (*formerly Iterum Therapeutics Limited*):

We consent to the use of our report dated March 9, 2018, except as for the effects of the Reverse Share Split discussed in Note 12 to the consolidated financial statements, as to which the date is May 16, 2018 with respect to the consolidated balance sheets of Iterum Therapeutics plc (*formerly Iterum Therapeutics Limited*) as of December 31, 2017 and 2016, and the related consolidated statements of operations and comprehensive loss, changes in convertible preferred shares and shareholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2017, and the related notes (collectively, the consolidated financial statements), included herein and to the reference to our firm under the heading "Experts" in the prospectus.

/s/ KPMG

Dublin, Ireland
May 16, 2018