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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2024

OR

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

For the transition period from to

Commission File Number 001-38503

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

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

3 Dublin Landings,
North Wall Quay,
Dublin 1, Ireland
(Address of principal executive offices)

Not applicable
(Zip Code)

(+353) 1 903 8354
(Registrant's telephone number, including area code)

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

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

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

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

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

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

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

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. Yes ☐ No ☒.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. □

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). □

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the Registrant's ordinary shares, $0.01 par value per share, on the Nasdaq Capital Market on June 30, 2024, the last business day of the Registrant's most recently completed second fiscal quarter was $19.2 million.

The number of shares of Registrant's ordinary shares outstanding as of February 6, 2025 was 34,581,405.

Table of Contents

		Page
PART I		
Item 1.	Business	1
Item 1A.	Risk Factors	42
Item 1B.	Unresolved Staff Comments	98
Item IC.	Cybersecurity	98
Item 2.	Properties	99
Item 3.	Legal Proceedings	99
Item 4.	Mine Safety Disclosures	99
PART II		
Item 5.	Market for Registrant's Common Equity, Related Shareholder Matters and Issuer Purchases of Equity Securities	100
Item 6.	[Reserved]	100
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	101
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	114
Item 8.	Financial Statements and Supplementary Data	115
Item 9.	Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	149
Item 9A.	Controls and Procedures	149
Item 9B.	Other Information	149
Item 9C.	Disclosure Regarding Foreign Jurisdictions that Prevent Inspections	150
PART III		
Item 10.	Directors, Executive Officers and Corporate Governance	151
Item 11.	Executive Compensation	153
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters	162
Item 13.	Certain Relationships and Related Transactions, and Director Independence	164
Item 14.	Principal Accounting Fees and Services	167
PART IV		
Item 15.	Exhibits, Financial Statement Schedules	168
Item 16	Form 10-K Summary	173

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

- our use of cash reserves;
- our ability to continue as a going concern;
- the design, initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the potential advantages of our product candidates;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization of our product candidates, if approved;
- our manufacturing plans;
- our sales, marketing and distribution capabilities and strategy;
- the market opportunity for and the potential market acceptance of ORLYNVAH™ for uncomplicated urinary tract infections caused by certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options;
- 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 and 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 and our ability to defend and enforce any such intellectual property rights;
- our ability to enter into strategic arrangements, collaborations and/or commercial partnerships in the United States and other territories and the potential benefits of such arrangements;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- our expectations regarding how far into the future our cash on hand will fund our ongoing operations;
- our financial performance;
- developments relating to our competitors and our industry;
- our ability to maintain compliance with listing requirements of the Nasdaq Capital Market;
- the impact of general economic conditions, including inflation;
- our strategic process to sell, license, or otherwise dispose of our rights to ORLYNVAH™ to maximize value for our stakeholders and the outcome, impact, effects and results of our pursuit of strategic alternatives, including the terms, timing, structure, value, benefits and costs of any strategic process and our ability to complete one at all; and
- our ability to successfully prepare and implement commercialization plans for ORLYNVAH™, with a commercial partner or directly, including our ability to build and maintain a sales force and prepare for commercial launch of ORLYNVAH™, if we are unsuccessful at entering into or completing a strategic transaction.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in "Risk Factors" and elsewhere in this Annual Report. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all

factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Annual Report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

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

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

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

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

SUMMARY OF RISK FACTORS

Below is a summary of the principal factors that make an investment in our ordinary shares speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below in the "Risk Factors" section of this Annual Report on Form 10-K, and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the SEC before making investment decisions regarding our ordinary shares. These risks include the following:

•Our exploration and pursuit of strategic alternatives may not be successful. Our board of directors, after receiving positive data from our REnewed ASsessment of Sulopenem in uncomplicated urinary tract infections caused by Resistant Enterobacterales (REASSURE) clinical trial in January 2024, determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing stakeholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Following receipt of U.S. Food and Drug Administration (FDA) approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized. Despite our plan to devote significant efforts to identify and evaluate potential strategic options, the process may not result in any definitive offer to consummate such a transaction, or, if we receive such a definitive offer, the terms may not be as favorable as anticipated or may not result in the execution or approval of a definitive agreement. Even if we enter into a definitive agreement, we may not be successful in completing a transaction or, if we complete such a transaction, it may not enhance shareholder value or deliver expected benefits. Since we may not ultimately pursue or consummate a strategic transaction, we have begun to evaluate other options for maximizing the value of ORLYNVAH™ including opportunities to raise capital to potentially support commercialization efforts.

•In the event that we do not successfully identify a viable strategic option, or consummate such a transaction, or if we are unable to raise sufficient capital to fund operations and commercialize ORLYNVAH™, our board of directors may determine that a liquidation and dissolution of our business approved by shareholders is the best method to seek to maximize shareholder value. In such an event, the amount of cash available for distribution to our shareholders, if any, will depend heavily on the timing of such liquidation as well as the amount of cash that will need to be reserved for commitments and contingent liabilities.

•We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of December 31, 2024, we had $24.1 million of cash and cash equivalents. Subsequently, we have paid off debt and sold additional ordinary shares under the "at the market offering" agreement with H.C. Wainwright & Co. LLC. Based on our available cash resources, we do not believe that our existing cash and cash equivalents will enable us to fund our operating expenses for the next 12 months from the date of filing of this Annual Report on Form 10-K.

•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. As of December 31, 2024, we had an accumulated deficit of $486.1 million.

•We will require additional capital to fund our operations. If we fail to obtain financing when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

•We are heavily dependent on the success of our sulopenem program, and our ability to successfully commercialize ORLYNVAH™ and to develop, obtain additional marketing approvals for and successfully commercialize oral sulopenem and IV sulopenem in jurisdictions outside the United States and/or for other indications. If we are unable to achieve and sustain profitability, the market value of our ordinary shares will likely decline.

•In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Should we seek to commercialize ORLYNVAH™, we will be heavily dependent on the success of ORLYNVAH™, which the FDA has approved for the treatment of uncomplicated urinary tract infections caused by certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options. Any failure to successfully commercialize ORLYNVAH™ or inability to obtain marketing approval for any other product candidates, or significant delays in doing so, will materially harm our business.

•Serious adverse events or undesirable side effects or other unexpected properties of ORLYNVAH™, 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.

•Even though ORLYNVAH™ has obtained regulatory approval in the United States and we may obtain regulatory approval for other product candidates, they 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.

•We currently have no commercial organization. If we are unable to establish and maintain sales, marketing and distribution capabilities, enter into sales, marketing and distribution agreements with third parties, or enter into a strategic transaction with a partner that has established commercial capabilities in the United States, ORLYNVAH™ may not be successfully commercialized.

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

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

•We rely heavily on the exclusive license agreement with Pfizer Inc. (Pfizer), for the patent rights and know-how required for the development of sulopenem and to commercialize ORLYNVAH™ and the know-how required to develop the IV formulation of sulopenem. If we fail to comply with our obligations in our agreement with Pfizer, we could lose such rights that are important to our business.

•If we are unable to obtain and maintain patent protection or other intellectual property rights for ORLYNVAH™ 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 commercialize ORLYNVAH™ or develop and commercialize any other product candidates or technology or otherwise compete effectively in our markets.

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

•The volatility of our shares and shareholder base may hinder or prevent us from engaging in beneficial corporate initiatives. Our shareholder base is comprised of a large number of retail (or non-institutional) investors, which creates more volatility since shares change hands frequently. As a result, there can be a significant turnover of shareholders between the record date and the meeting date which makes it harder to get shareholders to vote. While we make every effort to engage retail investors, such efforts can be expensive and the frequent turnover creates logistical issues for obtaining shareholder approval. Further, retail investors tend to be less likely to vote in comparison to institutional investors. Failure to secure sufficient votes may impede our ability to move forward with initiatives that are intended to grow the business and create shareholder value or prevent us from engaging in such initiatives at all.

PART I

Item 1. Business.

Overview

We are a pharmaceutical company dedicated to maximizing the commercial potential of ORLYNVAH™, the first oral branded penem available in the United States and 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 developed sulopenem in an oral tablet formulation, sulopenem etzadroxil-probenecid, which we refer to herein as oral sulopenem or ORLYNVAH™, as the context so requires. We refer to sulopenem delivered intravenously as sulopenem and, sulopenem together with oral sulopenem/ORLYNVAH™, as our sulopenem program. We believe that sulopenem and ORLYNVAH™ 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 exclusively license from Pfizer Inc. (Pfizer) two U.S. patents and three foreign patents, including one U.S. patent directed to composition of matter of sulopenem etzadroxil, which is projected to expire in 2029, subject to potential extension under the Drug Price Competition and Patent Term Restoration Act of 1984, (Hatch-Waxman Act), to 2034, and three foreign patents related to sulopenem etzadroxil. We own four U.S. patents, one Japanese patent, one Korean patent and one Australian patent, with one U.S. patent, the Japanese patent, the Korean patent and the Australian patent directed to the composition of the bilayer tablet of oral sulopenem and its related preparations and/or uses. Two U.S. patents are directed to the method of use of oral sulopenem in treating multiple diseases, including uUTIs. One U.S. patent is directed to the method of use of sulopenem etzadroxil, probenecid, and valproic acid in treating multiple diseases. The patents owned by us are scheduled to expire between 2039 and 2041, excluding any additional term for patent adjustments or patent term extensions. We also own three pending U.S. patent applications, and 26 pending foreign patent applications, which collectively cover uses of sulopenem and probenecid and bilayer tablets of sulopenem etzadroxil and probenecid. We were notified that one pending Canadian patent application, which is directed to the bilayer tablet of oral sulopenem and its related preparations and/or uses, was allowed in 2024. This Notice of Allowance concludes the substantive examination of the patent application and will result in the issuance of a Canadian patent after administrative processes are completed. One pending Australian patent application, which is directed to the use of sulopenem etzadroxil and probenecid in treating multiple diseases, including uncomplicated urinary tract infection (uUTI), was also recently allowed. Any U.S. or foreign patents issuing from the pending applications are projected to expire between 2039 and 2041, excluding any additional term for patent adjustments or patent term extensions.

Recent Developments

On October 25, 2024, we received approval from the U.S. Food and Drug Administration (FDA) of our New Drug Application (NDA) for ORLYNVAH™ for the treatment of uUTI in adult women caused by the designated microorganisms *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women with limited or no alternative oral antibacterial treatment options.

After receiving positive data from our Phase 3 clinical trial known as REnewed ASsessment of Sulopenem in uUTI caused by Resistant Enterobacterales (REASSURE) in January 2024, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing stakeholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating various strategic alternatives. Following receipt of FDA approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized. In the event our strategic process to sell, license, or otherwise dispose of our rights to ORLYNVAH™ to maximize value for our stakeholders, does not result in any type of transaction, we are considering our options for commercializing ORLYNVAH™ in the United States with a commercial partner and/or on our own with a targeted sales force in the community setting.

Our Strategy

Since inception, our strategy has been to develop and commercialize our sulopenem program for multiple indications, and in the long term to build a market-leading anti-infective business. While we have been focused on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing stakeholder value and engaged a financial advisor to assist management and the board in evaluating strategic alternatives, we cannot provide any commitment regarding when or if this strategic process will result in any type of transaction however, and no assurance can be given that we will determine to pursue a potential sale, licensing arrangement or other disposition of our rights to sulopenem. Since we may not ultimately pursue or consummate a strategic

transaction, we have begun to evaluate other options for maximizing the value of ORLYNVAH™, which may include raising capital to support the commercialization of ORLYNVAH™.

As such, our strategy going forward may include some or all of the following elements:

•***Maximize commercial potential of ORLYNVAH™.*** We may seek a commercial partner and/or seek to directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Outside of the United States, we continue to evaluate other options to maximize the value of our sulopenem program.

•***Consider regulatory strategy outside the United States.*** We are considering the timing of a potential submission of a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA).

•***Pursue the development of our sulopenem program in additional indications***. In the future, we may also pursue development of our sulopenem program in additional indications in adults and children, including complicated urinary tract infections (cUTIs), community acquired bacterial pneumonia, non-tuberculous mycobacterial pulmonary disease, complicated intra-abdominal infections (cIAIs), bacterial prostatitis, gonorrhea, diabetic foot infection and bone and joint infection, as well as new formulations to support these indications.

•***Build a portfolio of differentiated anti-infective products***. We may seek 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.

Sulopenem Program, Clinical and Regulatory Status

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

During the third quarter of 2018, we initiated three clinical trials in our Phase 3 development program which included: (i) a Phase 3 uncomplicated uUTI clinical trial, known as Sulopenem for Resistant Enterobacteriaceae (SURE) 1, comparing ORLYNVAH™ to oral ciprofloxacin in women with uUTI, (ii) a Phase 3 cUTI clinical trial known as SURE 2, comparing IV sulopenem followed by ORLYNVAH™ to IV ertapenem followed by oral ciprofloxacin in adults with cUTI; and (iii) a Phase 3 cIAI clinical trial known as SURE 3, comparing IV sulopenem followed by ORLYNVAH™ to IV ertapenem followed by a combination of oral ciprofloxacin and oral metronidazole in adults with cIAI. In the second quarter of 2020, we announced the results of our Phase 3 clinical trials in cUTI (SURE 2) and uUTI (SURE 1). In the cUTI trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapies with the difference in response rates driven almost entirely by higher rates of asymptomatic bacteriuria on the sulopenem IV to oral sulopenem arm relative to the ertapenem IV to oral ciprofloxacin arm, only evident at the test of cure visit. The rates of patients receiving additional antibiotics or with residual cUTI symptoms were similar between therapies. Similarly, in the uUTI trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to ciprofloxacin in the population of patients with baseline pathogens susceptible to ciprofloxacin driven to a large degree by a greater amount of asymptomatic bacteriuria in the sulopenem treated patients at the test of cure visit relative to those receiving ciprofloxacin. However, in the uUTI trial, in the population of patients with baseline pathogens resistant to quinolones, sulopenem achieved the related primary endpoint by demonstrating statistical significance in the overall response rate by treatment arm in the ciprofloxacin-resistant population, providing evidence of a treatment effect in patients with uUTI. Based on discussions with the FDA at a pre-NDA meeting in September 2020 and previous correspondence with the FDA, we submitted an NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020 and the FDA accepted the application for review in January 2021. We received a Complete Response Letter (CRL) from the FDA on July 23, 2021 in respect of our NDA. The CRL provided that the FDA had completed its review of the NDA and had determined that it could not approve the NDA in its present form. The CRL further provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone, and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022, we reached an agreement with the FDA under the Special Protocol Assessment (SPA) process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for ORLYNVAH™ for the treatment of uUTIs and commenced enrollment in that clinical trial, known as REnewed ASsessment of Sulopenem in uUTI caused by Resistant Enterobacterales (REASSURE), in October 2022. The study was designed as a non-inferiority trial comparing ORLYNVAH™ and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. In October 2023 we completed enrollment in the REASSURE clinical trial, enrolling 2,222 patients. In January 2024, we announced that ORLYNVAH™ met the primary endpoint of statistical non-inferiority to Augmentin® in the Augmentin®-susceptible population, and demonstrated statistically significant superiority versus Augmentin® in the Augmentin® susceptible population, in the REASSURE clinical trial. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical pharmacokinetic-pharmacodynamic

(PK/PD) studies to support dose selection for the proposed treatment indication(s), which we completed as recommended by the FDA. We resubmitted our NDA to the FDA for ORLYNVAH™ for the treatment of uUTIs in April 2024. In May 2024, we received a notice from the FDA acknowledging receipt of the resubmission of the NDA and indicating that the FDA deemed our NDA resubmission to be a Class II complete response under the Prescription Drug User Fee Act (PDUFA), which has a six-month review period from the date of resubmission. On October 25, 2024, we received approval from the FDA of our NDA for ORLYNVAH™ for the treatment of uncomplicated urinary tract infections caused by the designated microorganisms *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women with limited or no alternative oral antibacterial treatment options.

The Medical Need

Urinary Tract and Intra-Abdominal Infections

Urinary tract 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.

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 15 million emergency room and office visits for symptoms of urinary tract infections (UTIs) and approximately 33 million uUTIs in the United States annually, with approximately 30% of those infections caused by a quinolone non-susceptible organism, and approximately 1% of infections are caused by pathogens that are resistant to all commonly available classes of oral antibiotics. Based on market research, physicians estimated that approximately 35% of these patients are at elevated risk for treatment failure. Proper antibiotic treatment of drug-resistant infections in this group is particularly important due to the risks associated with treatment failure. At-risk patients were defined in the research as patients with recurrent UTIs, elderly patients, patients who have a suspected or confirmed drug-resistant infection, patients with comorbidities (e.g., Diabetes mellitus) or that are immunocompromised, patients that have had a recent hospitalization, patients with a history of prior antibiotic failure and patients in a long-term care setting. Treatment failures pose significant clinical and economic challenges to the healthcare system. In 2022, a retrospective database analysis of 5,395 evaluable outpatient UTI episodes revealed that 22% of patients received an antibiotic to which the pathogen was resistant *in vitro*, and those patients were almost twice as likely to require a second prescription (34% versus 19%) or be hospitalized (15% versus 8%) within 28 days of the initial prescription fill compared to patients who received an antibiotic to which the pathogen was susceptible. 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.

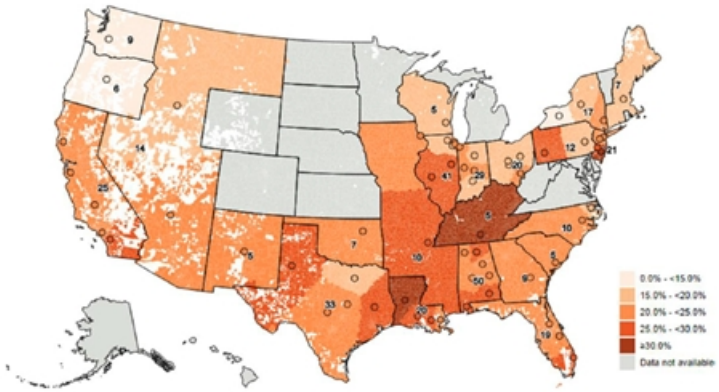
Antimicrobial Resistance Is Increasing

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 2019, approximately 40% of oral prescriptions for UTIs written in the United States were for fluoroquinolones or trimethoprim-sulfamethoxazole. In hospitals, fluoroquinolones have greater than 30% resistance to *E. coli* in approximately half the states in the United States, and have greater than 25% resistance rates in nearly 80% of the states. According to national data published by the Centers for Disease Control and Prevention (CDC), fluoroquinolones had greater than 33% resistance to *E. coli* in the United States in 2019 in hospitalized patients, and in 2020, the national resistance rate of *E. coli* to fluoroquinolones increased to 35.2%. Further, the national resistance rate of *E. coli* to cephalosporins, which is a common marker for extended spectrum ß-lactamases (ESBL)-producing *E. coli,* was estimated to be approximately 13% for the combined years of 2011 to 2015, and in 2020, and the resistance rate to cephalosporins was reported to be 24.7% by the CDC. 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%. In a 2022 special report from the CDC describing the U.S. impact of COVID-19 on antimicrobial resistance, rates of ESBL cases increased an estimated 10% from 2019 through 2020, primarily driven by a 32% increase in hospital-onset versus 7% increase in community-onset infections. Data reported by the European Antimicrobial Resistance Surveillance Network (EARS-Net) in Europe demonstrate that in 2022, the prevalence of quinolone resistant *E. coli* and *E. coli* resistant to third generation cephalosporins is 22%

(European Union (EU)/European Economic Area (EEA) country range 9.9-46.4%) and 14.3% (EU/EEA country range 5.8-40.2%), respectively. The prevalence of *E. coli* with combined resistance to third generation cephalosporins, fluoroquinolones, and aminoglycosides is 5.1% (EU/EEA country range 1.5-14.2%).

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. A recent nationwide database study that evaluated trends in antibiotic resistance in urinary Enterobacterales isolates from ambulatory patients in the United States revealed that antimicrobial resistance was common in urinary Enterobacterales isolates. Isolates with an ESBL-producing phenotype increased by about 30% between 2011 and 2020, and significant increases were also observed in nitrofurantoin non-susceptible Enterobacterales isolates. Resistance rates for all four antibiotic classes (fluoroquinolones, trimethoprim-sulfamethoxazole, nitrofurantoin and β-lactams), were higher than thresholds recommended for use as empiric therapy. 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

Based on market research, there are approximately 40 million total prescriptions for uUTIs (including repeat patients) in the United States annually with approximately two-thirds or 26 million of those prescriptions written for patients that are at elevated risk for treatment failure, based on market research. Proper antibiotic treatment of drug-resistant infections in this group is particularly important due to the consequences associated with treatment failure. At-risk patients were defined in the research as patients with recurrent UTIs, elderly patients, patients who have a suspected or confirmed drug-resistant infection, patients with comorbidities (e.g., Diabetes mellitus) or that are immunocompromised, patients that have had a recent hospitalization, patients with a history of prior antibiotic failure and patients in a long-term care setting.

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

Limited Treatment Options

In addition to worsening antibiotic resistance, many of the antibiotics currently used for first-line empiric oral treatment of uUTIs, such as nitrofurantoin and trimethoprim-sulfamethoxazole, suffer from significant safety and tolerability concerns. Pulmonary fibrosis and diffuse interstitial pneumonitis have been observed in patients treated with nitrofurantoin, which is contraindicated in

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

The limited oral antibiotic treatment options for patients with uUTIs can sometimes result in hospitalization to facilitate administration of IV antibiotics for patients whose infection progresses. In addition, some patients whose uUTI remains uncomplicated may require hospital admission for IV therapy. For patients with cUTIs, the lack of effective oral stepdown options, and the paucity of new treatment options, which is demonstrated by the fact that none of the most commonly used oral agents were initially approved by the FDA in the last two decades, results in the potential for lengthy hospital stays or insertion of a peripherally inserted central catheter to facilitate administration of IV antibiotics, even for some patients with relatively straightforward infections. Therefore, based both on the epidemiology described above and recent discussions with practicing clinicians and pharmacists, we believe there is a pressing need for a novel oral antibacterial therapy for UTI, both complicated and uncomplicated, that has potent activity against ESBL producing and quinolone resistant gram-negative organisms. ORLYNVAH™ is indicated for the treatment of uUTIs in adult women caused by *Escherichia coli*, *Klebsiella pneumonia* or *Proteus mirabilis* (>95% of uUTIs). ORLYNVAH™ has the potential therefore, to be an important new oral treatment for clinicians and patients who have limited or no alternative oral antibiotic treatment options.

The Challenge of Developing Antibiotics

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

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

The Solution to Rising Resistance

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

These new agents will need to:

•kill the organisms responsible for the actual infection;

•target a specific bacterial function and overcome the existing resistance mechanisms around that function;

•be powerful enough to require a minimal amount of drug to kill the organism at the site of infection; and

•be delivered to a patient in a manner which is safe, tolerable and convenient.

For the last 30 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. ORLYNVAH™ is the first and only FDA-approved oral penem and has the potential therefore, to be an important new oral treatment for clinicians and patients who have limited or no alternative oral antibiotic treatment options.

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, ORLYNVAH™ can be provided as a tablet, offering an option for care of those with a culture proven or suspected MDR pathogen, namely *Escherichia coli*, *Klebsiella pneumonia* or *Proteus mirabilis*, 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 ORLYNVAH™, potentially enabling the patient to leave the hospital.

Potential Advantages of ORLYNVAH™ and Sulopenem

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

Sulopenem's differentiating characteristics include:

•***Activity as an oral agent and favorable pharmacokinetic profile.*** Sulopenem is the active moiety with antibacterial activity. ORLYNVAH™ is a prodrug specifically selected among many other prodrug candidates because it enables the absorption of sulopenem from the gastrointestinal tract. It is this oral agent, sulopenem etzadroxil, combined with probenecid that we believe meets an urgent medical need to allow patients with resistant pathogens to be treated safely in the community, as well as allowing hospitalized patients to continue their treatment at home. ORLYNVAH™ 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.

•***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.*** In our completed Phase 3 program, sulopenem and ORLYNVAH™ were well tolerated. In the cIAI clinical trial, among the 668 patients treated, treatment-related adverse events were observed in 6.0% and 5.1% of patients on sulopenem and ertapenem, respectively, with the most commonly reported drug-related adverse event being diarrhea, which was observed in 4.5% and 2.4% of patients on sulopenem and ertapenem, respectively. Discontinuations from treatment were uncommon for both regimens, occurring in 1.5% of patients on sulopenem and 2.1% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 7.5% of patients on sulopenem and 3.6% of patients on ertapenem. In the cUTI trial, patients received either sulopenem followed by ORLYNVAH™, if eligible for oral therapy, or ertapenem IV followed by ciprofloxacin or amoxicillin-clavulanate, if eligible for oral therapy. Among 1,392 treated patients, treatment-related adverse events were observed in 6.0% and 9.2% of patients on sulopenem and

ertapenem, respectively, with the most commonly reported adverse events being headache (3.0% and 2.2%), diarrhea (2.7% and 3.0%) and nausea (1.3% and 1.6%), on sulopenem and ertapenem, respectively. Discontinuations from treatment were uncommon for both regimens, occurring in 0.4% of patients on sulopenem and 0.6% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 2.0% of patients on sulopenem and 0.9% of patients on ertapenem. In the uUTI trial (SURE 1), patients received either ORLYNVAH™ or ciprofloxacin. Among 1,660 treated patients, treatment related adverse events were observed in 17.0% and 6.2% of patients on sulopenem and ciprofloxacin, respectively. The most commonly reported adverse events were diarrhea (12.4% and 2.5%), nausea (3.7% and 3.6%), and headache (2.2% and 2.2%), for sulopenem and ciprofloxacin patients, respectively. The difference in adverse events was driven by diarrhea which, in the majority of patients, was mild and self-limited. Overall discontinuations due to adverse events were uncommon on both regimens and were seen in 1.6% of patients on sulopenem and 1.0% of patients on ciprofloxacin. Serious adverse events were seen in 0.7% of patients on sulopenem with one drug-related serious adverse event due to transient angioedema and 0.2% of patients on ciprofloxacin with no drug-related serious adverse event. In the REASSURE clinical trial, patients received either ORLYNVAH™ or Augmentin®. Among 2,214 treated patients, treatment related adverse events were observed in 18.9% and 12.3% of patients on ORLYNVAH™ and Augmentin®, respectively. The most commonly reported adverse events were diarrhea (8.1% and 4.1%), nausea (4.3% and 2.9%), and headache (2.2% and 1.5%), for ORLYNVAH™ and Augmentin® patients, respectively. The difference in adverse events was driven by diarrhea which, in the majority of patients, was mild and self-limited. Overall discontinuations due to adverse events were uncommon on both regimens and were seen in 0.7% of patients on ORLYNVAH™ and 0.4% of patients on Augmentin®. Serious adverse events were seen in 0.0% of patients on ORLYNVAH™ and 0.5% of patients on Augmentin® with no drug-related serious adverse event.

•***Availability of an IV formulation.*** 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 offer both important formulations as therapeutic options. There is no IV formulation currently approved.

•***Established 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 have registered two different contract manufacturing organizations to manufacture the active pharmaceutical ingredient (API) for ORLYNVAH™. We have API for commercial launch of ORLYNVAH™. Subject to the outcome of our strategic process and our ability to raise sufficient capital, should we decide to build a commercial infrastructure to launch ORLYNVAH™ in the United States, we will initially rely on a single third-party facility to manufacture all of our sulopenem tablets. Given the importance of ORLYNVAH™ to our potential commercial results, we will consider establishing additional sources in the future if we pursue commercializing ORLYNVAH™ in the United States.

Market Opportunity for ORLYNVAH™

We expect the commercial opportunity for ORLYNVAH™ to be substantial with initial focus on the treatment of uUTIs in elevated risk patients caused by drug-resistant pathogens in the community. We estimate that approximately 30% of uUTIs in the United States are caused by quinolone non-susceptible pathogens, and approximately 1% of infections are caused by pathogens that are resistant to all commonly available classes of oral antibiotics.

Acute cystitis remains one of the most common indications for prescribing antimicrobials to otherwise healthy women, resulting in as many as 15 million office or emergency room visits in the United States annually, according to a review published in 2015. Up to 50% of all women experience one episode by 32 years of age. In addition, there are approximately 3.6 million patients a year in the United States for the more serious cases of cUTI.

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

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

We believe ORLYNVAH™'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.

Clinical Development Program

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

Both sulopenem and ORLYNVAH™ have received Qualified Infectious Diseases Products (QIDP) designation status for the indications of uUTI, cUTI and cIAI as well as for community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. QIDP designation status for other indications is also possible given the coverage of gram-negative and gram-positive bacteria by sulopenem, pending submission of additional documentation and acceptance by the FDA. We had 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 non-clinical study requirements, the design of the Phase 1 and Phase 3 clinical trials, the pediatric development plan, as well as support for the proposed chemistry, manufacturing, and controls (CMC) development activities through production of commercial supplies. The Phase 3 clinical trials for treatment of cIAI, cUTI and uUTI received SPA agreements with the FDA. All three Phase 3 clinical trials were initiated in the third quarter of 2018 and completed enrollment by the end of 2019. In December 2019, we announced that sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy for the cIAI trial. EMA Scientific Advice received by us, consistent with the existing guidance for this indication, supports an endpoint assessed earlier than the primary study endpoint and a non-inferiority margin of -12.5%. In the second quarter of 2020, we announced the results of our Phase 3 clinical trials in cUTI and uUTI. In the cUTI trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapies, with the difference in response rates driven almost entirely by higher rates of asymptomatic bacteriuria on the sulopenem IV to oral sulopenem arm relative to the ertapenem IV to oral ciprofloxacin arm, only evident at the test of cure visit. The rates of patients receiving additional antibiotics or with residual cUTI symptoms were similar between therapies. Similarly, in the uUTI trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to ciprofloxacin in the population of patients with baseline pathogens susceptible to ciprofloxacin, driven to a large degree by a greater amount of asymptomatic bacteriuria in the sulopenem treated patients at the test of cure visit relative to those receiving ciprofloxacin. However, in the uUTI trial, in the population of patients with baseline pathogens resistant to quinolones, sulopenem achieved the related primary endpoint by demonstrating superiority to ciprofloxacin, providing evidence of a treatment effect in patients with uUTI. Notwithstanding failure to meet the endpoints described above, in all three Phase 3 clinical trials, at all timepoints measured, the clinical response to sulopenem and/or oral sulopenem was similar to the comparator regimen (non-inferior), except in the instance of the quinolone non-susceptible population in the Phase 3 uUTI trial in which oral sulopenem was statistically superior. Further, we believe the secondary supporting analyses and safety data support the potential of sulopenem in the treatment of multi-drug resistant infections. Based on discussions with the FDA at a pre-NDA meeting in September 2020 and previous correspondence with the FDA, we submitted an NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020 and the FDA accepted the application for review in January 2021. As described above, we received a CRL from the FDA on July 23, 2021 in respect of our NDA. The CRL provided that the FDA had completed its review of the NDA and had determined that it could not approve the NDA in its present form. The CRL further provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study was designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. In October 2023 we completed enrollment in the REASSURE clinical trial, enrolling 2,222 patients. In January 2024, we announced that ORLYNVAH™ met the primary endpoint of statistical non-inferiority to Augmentin® in the Augmentin®-susceptible population, and demonstrated statistically significant superiority versus Augmentin® in the Augmentin® susceptible population, in the REASSURE clinical trial. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical PK/PD studies to support dose selection for the proposed treatment indication(s), which we completed as recommended by the FDA. We resubmitted our NDA to the FDA in April 2024 and received approval for ORLYNVAH™ by the FDA in October 2024 for the treatment of uncomplicated uUTIs caused by certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options.

Microbiology Surveillance Data

Sulopenem has demonstrated potent *in vitro* activity, as defined by its minimum inhibitory concentration (MIC), against nearly all genera of Enterobacteriaceae, in anaerobes such as Bacteroides, Prevotella, Porphyromonas, Fusobacterium and Peptostreptococcus, gram-positive organisms including methicillin-susceptible staphylococci, *Streptococcus pyogenes* and *Streptococcus pneumoniae*, as well as other community respiratory pathogens such as *Haemophilus influenzae* and *Moraxella catarrhalis*. The MIC is a measure used to describe the results of an *in vitro* assay in which a fixed number of a strain of bacteria are added to a 96-well plate and increasing concentrations of antibiotic are sequentially added to the wells. The concentration of antibiotic which inhibits growth of the bacteria in a well is considered the MIC. When looking across a collection of many strains of a species of bacteria, the MIC_{90} is the lowest concentration of antibiotic at which 90% of the strains are inhibited. Sulopenem lacks *in vitro* activity ($MIC_{90} \geq 16$ µg/mL) against the oxidative non-fermenting pathogens such as *Pseudomonas aeruginosa*, *Acinetobacter baumanii*, *Burkholderia cepacia*, and *Stenotrophomonas maltophilia*. Given its lack of potency against *Pseudomonas aeruginosa*, its use in treatment of infections caused by pathogenic Enterobacteriaceae should not select for pseudomonas resistant to carbapenems, as can occur with imipenem and meropenem. For various species of enterococci, the MIC_{90} values were 4 to ≥ 64 µg/mL. Methicillin-resistant staphylococci also have high MIC values.

The table below highlights the MIC_{50} and MIC_{90} of key target pathogens collected by JMI Laboratories in 2019 responsible for the infections studied in our Phase 3 program.

Organism Class	**N**	**MIC_{50} (µg/mL)**	**MIC_{90} (µg/mL)**
E. coli	983	0.03	0.03
ESBL negative	813	0.03	0.03
ESBL positive	170	0.03	0.06
Klebsiella spp.	347	0.03	0.12
ESBL negative	224	0.03	0.06
ESBL positive	49	0.06	1
P. mirabilis	91	0.25	0.25
E. cloacae species complex	110	0.12	0.5
C. koseri	9	0.03	-
S. marcescens	36	0.5	2
Gram-negative anaerobes	287	0.12	1

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 = 983**		***K. pneumoniae*** **N = 273**		***P. mirabilis*** **N = 91**	
Penem Class:	**MIC_{90} (µg/mL)**	**%S***	**MIC_{90} (µg/mL)**	**%S***	**MIC_{90} (µg/mL)**	**%S***
Sulopenem	0.03	-	0.06	-	0.25	-
Ertapenem	0.03	99.7	0.06	97.1	0.015	100
Imipenem	≤0.12	99.9	0.5	98.5	2	38.5
Meropenem	0.03	99.9	0.03	98.5	0.12	100
Oral Agents Currently on Market:						
Nitrofurantoin	32	96	>64	23.1	>64	2.2
Ciprofloxacin	>16	70.3	4	78.3	>16	74.7
Trimethoprim-Sulfamethoxazole	>16	65.9	>16	80.2	>16	80
Amoxicillin-Clavulanate	16	80.3	16	85.3	2	97.8

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. See below, susceptibility breakpoints recommended by the FDA for ORLYNVAH™.

FDA Susceptibility Breakpoints for ORLYNVAH™

The FDA-recommended broth microdilution (MIC) and disk diffusion interpretive criteria (breakpoints) for ORLYNVAH™ are set out in the table below:

	Broth Microdilution Method (MIC)			**Disk Diffusion Method Zone Diameter (BP)**		
Indicated Pathogens	**Susceptible (S) mcg/mL**	**Intermediate (I) mcg/mL**	**Resistant (R) mcg/mL**	**Susceptible(S) mm**	**Intermediate(I) mm**	**Resistant (R) mm**
E. coli	≤0.25	0.5	≥1.0	≥19	16-18	≤15
K. pneumoniae	≤0.25	0.5	≥1.0	≥19	16-18	≤15
P. mirabilis	≤0.25	0.5	≥1.0	≥19	16-18	≤15

BPs = break points
MIC = minimum inhibitory concentration

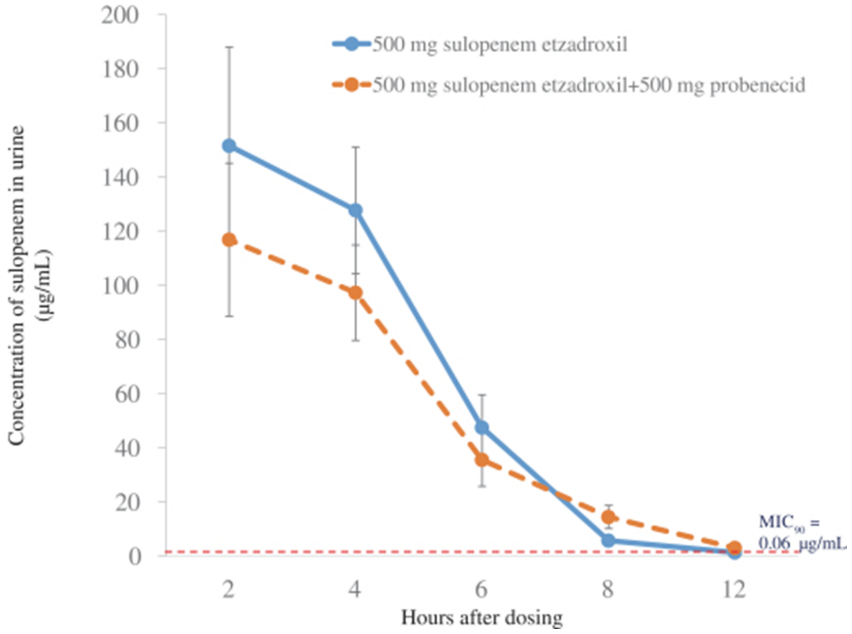
ORLYNVAH™

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

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

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

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



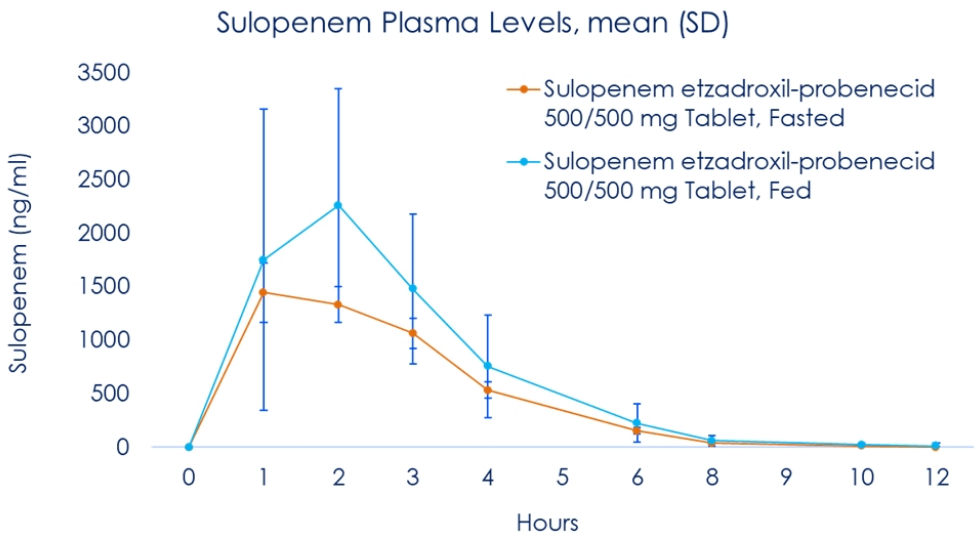
In IT001-102, we evaluated sulopenem etzadroxil administered with and without probenecid in a randomized cross-over trial in healthy volunteers in a fasted state. Subjects receiving sulopenem etzadroxil in a powder-in-a-bottle formulation co-administered with a separate tablet of probenecid demonstrated an increase in the time over MIC (of a 12 hour dosing interval) and AUC of sulopenem, as shown in the table below.

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

N = number of subjects; C_{max} = maximum plasma concentration; $AUC_{0-¥}$ = area under the curve from the initiation of dosing extrapolated through infinite time

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

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



A Phase 1 drug interaction study with itraconazole demonstrated no interaction. An additional Phase 1 drug interaction study with valproic acid was also conducted which showed that IV sulopenem decreased the AUC and Cmax of valproic acid by approximately 33% and 28%, respectively, and oral sulopenem etzadroxil tablet without probenecid decreased valproic acid AUC and Cmax by approximately 25% and 19%, respectively, relative to valproic acid alone. These results are consistent with reports in the literature for other penem antibiotics co-administered with valproic acid. In contrast, multiple doses of sulopenem etzadroxil as the bilayer tablet had no effect on valproic acid AUC and Cmax relative to administration of valproic acid alone.

Sulopenem, IV Formulation

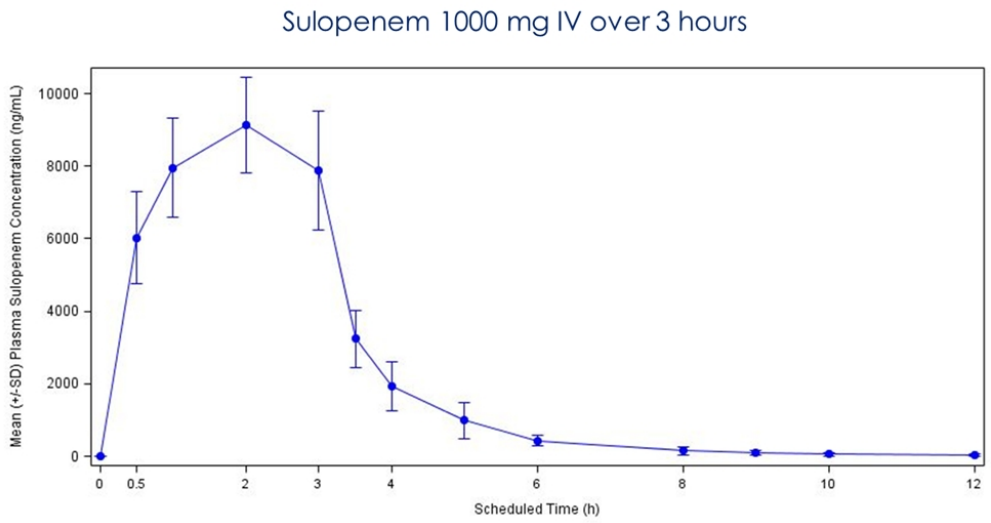
Doses of sulopenem up to 2800 mg as a single IV dose and 2000 mg BID, or twice daily, of sulopenem as IV over fourteen days were studied in three Phase 1 clinical trials in healthy adults, one study in patients with renal insufficiency in the United States and two Phase 1 clinical trials in Japan. Results 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 $_{0-¥}$ (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; $AUC_{0-¥}$ = area under the curve from the initiation of dosing extrapolated through infinite time; $T_{½}$ = half-life; CL_{total} = clearance (only measured on Day 14)

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

	N	Dose (mg)	Infusion duration (h)	C_{max} (µg/mL)	$AUC_{0-\infty}$ (µg hr/mL)	$T_{1/2}$ (h)
Day 1	12	1000	3	9.15	28.9	1.65



Modeling and Dose Selection

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

Phase 2 Clinical Trial with sulopenem and sulopenem etzadroxil

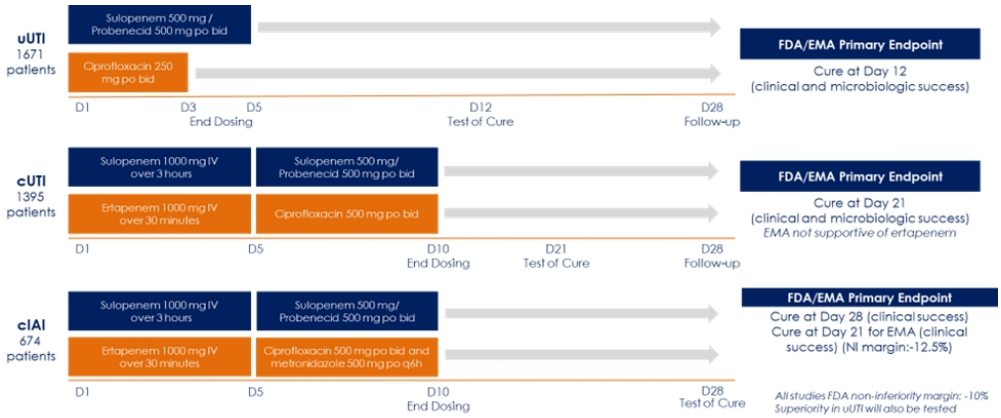
In 2009, Pfizer initiated a Phase 2, randomized, double-blind, double-dummy clinical trial in hospitalized patients with CAP comparing two regimens of IV sulopenem followed by sulopenem etzadroxil to ceftriaxone IV followed by amoxicillin-clavulanate. The sulopenem regimens were a single 600 mg IV dose of sulopenem followed by 1000 mg BID of sulopenem etzadroxil or a 600 mg of sulopenem for a minimum of four doses followed by 1000 mg BID of sulopenem etzadroxil. The clinical trial was terminated early for business reasons after 33 of 250 planned total patients were enrolled and treated. Clinical response rates at the test-of-cure visit (7–14 days after end of therapy) of the ITT patients were similar on each regimen (9/10, 9/11 and 7/12, on sulopenem single IV dose, sulopenem multidose IV and ceftriaxone, respectively). Treatment-emergent adverse events were reported in six subjects each in the sulopenem groups and eight subjects in the ceftriaxone group. The most common treatment-emergent adverse event was diarrhea, reported by a total of six subjects (two in each treatment group). Treatment related diarrhea was reported by one subject following

sulopenem single dose IV, and by a further two subjects following ceftriaxone. There was one treatment-related serious adverse event in the ceftriaxone group. There were no deaths reported in this clinical trial.

Phase 3 Clinical Trials - SURE 1, SURE 2, SURE 3

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 studies conducted by other sponsors, we negotiated SPA agreements for cUTI, cIAI and uUTI. All three Phase 3 clinical trials were initiated in the third quarter of 2018, and completed enrollment by the end of 2019. Oral sulopenem alone was studied for the treatment of outpatients with a uUTI. Oral sulopenem and sulopenem were studied for the treatment of cIAI and cUTI. 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 was defined by the lower limit of the confidence interval in the treatment difference of no more than -10%. The uUTI clinical trial also tested for superiority in the subset of patients with ciprofloxacin resistant pathogens at baseline. An open-label noncomparative treatment study of oral ciprofloxacin 250 mg twice daily for three days in uUTI patients was conducted to help characterize certain sample size assumptions as well as enable study logistics for this Phase 3 clinical trial. Patients in the cUTI and cIAI clinical trials received five days of sulopenem IV or comparator and then stepped down to two to five additional days of oral treatment with either oral sulopenem or ciprofloxacin. In the cIAI study, metronidazole was added to ciprofloxacin in the oral stepdown regimen.

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



In the uUTI trial (SURE 1), clinical outcome at the test-of-cure visit was noted as cure for those patients who are alive, who demonstrate resolution of the symptoms of uUTI 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. The primary endpoint was clinical and microbiologic response on Day 12 in the micro-MITT population. The micro-MITT population consists of those randomized patients who received a dose of study drug and had a gram-negative organism isolated in their urine. Two independent populations were prespecified and tested for an overall response of success at the test of cure (TOC) (Day 12): a) Superiority (286 patients): quinolone non-susceptible population assessed for superiority, defined as a p value <0.05, and b) Non-inferiority (785 patients): quinolone-susceptible population tested for non-inferiority, based on lower limit of 95% confidence interval for difference in microbiologic-modified intent to treat population being less than -10%.

Micro-MITT population		Sulopenem n/N (%)	Ciprofloxacin n/N (%)	Difference (95% CI)	P value
Quinolone Non-Susceptible Population	**Overall Response (TOC)**	92/147 (62.6%)	50/139 (36.0%)	26.6% (15.1, 37.4)	< 0.001
	Reason for Failure: ASB	27 (18.4%)	38 (27.3%)		
	Clinical Response (TOC)	122/147 (83.0%)	87/139 (62.6%)	20.4% (10.2, 30.4)	< 0.001
	Overall Response (EOT)	95/147 (64.6%)	42/139 (30.2%)	34.4% (23.1, 44.8)	< 0.001
Quinolone Susceptible Population	**Overall Response (TOC)**	247/370 (66.8%)	326/415 (78.6%)	-11.8% (-18.0, -5.6)	
	Reason for Failure: ASB	47 (12.7%)	16 (3.9%)		
	Clinical Response (TOC)	300/370 (81.1%)	349/415 (84.1%)	-3.0% (-8.4, 2.3)	
	Overall Response (EOT)	240/370 (64.9%)	271/415 (65.3%)	-0.4% (-7.1, 6.2)	
Combined *(Quinolone Susceptible and Quinolone Non-Susceptible Populations)*	**Overall Response (TOC)**	339/517 (65.6%)	376/554 (67.9%)	-2.3% (-7.9, 3.3)	
	Reason for Failure: ASB	74 (14.3%)	54 (9.7%)		
	Clinical Response (TOC)	422/517 (81.6%)	436/554 (78.7%)	2.9% (-1.9, 7.7)	
	Overall Response (EOT)	335/517 (64.8%)	313/554 (56.5%)	8.3% (2.4, 14.1)	0.006

ASB = asymptomatic bacteriuria; EOT = end of trial; TOC = test of cure

In the quinolone non-susceptible population, sulopenem is superior to ciprofloxacin. In the Combined TOC (quinolone susceptible and quinolone non-susceptible populations), sulopenem is non-inferior to ciprofloxacin; however, in the quinolone susceptible population only, sulopenem is not non-inferior due primarily to asymptomatic bacteriuria at TOC (at end of treatment, results are similar between arms).

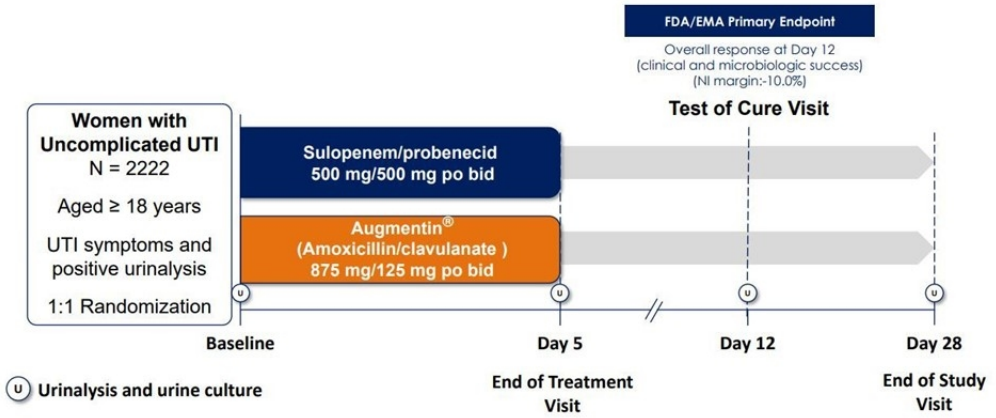
In the Phase 3 cUTI trial (SURE 2), clinical outcome at the test-of-cure visit was noted as cure for those patients who are alive, who demonstrate resolution of the symptoms of cUTI present at trial entry (and no new symptoms) such that no new antibiotics are required, as well as the demonstration that the bacterial pathogen(s) found at trial entry are reduced to $<10^3$ CFU/mL on urine culture on Day 21. The primary endpoint was clinical and microbiologic response on Day 21 in the micro-MITT population. The micro-MITT population consists of those randomized patients who received a dose of study drug and had a gram-negative organism isolated in their urine. In this population, the difference in outcomes was 6.1% with a 95% confidence interval on that difference of -12.0% to -0.1%. Non-inferiority for the primary endpoint required that the lower limit of the difference in the outcome rates be >-10%.

		Sulopenem	Ertapenem	Difference (95% Confidence Interval)
Test of Cure				
	microMITT	67.80%	73.90%	-6.1% (-12.0, -0.1)
	Clinically Evaluable	89.4%	88.4%	1.0% (-3.1, 5.1)
End of Treatment				
	Overall Response	86.70%	88.90%	-2.2% (-6.5, 2.2)

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

	Sulopenem	Ertapenem	Difference (95% Confidence Interval)
Test of Cure			
microMITT	85.5%	90.2%	-4.7% (-10.3, 1.0)
MITT	87.2%	90.0%	-2.9% (- 7.7, 2.0)
Clinically Evaluable	93.6%	95.7%	-2.0% (-5.7, 1.7)
Microbiologically Evaluable	92.5%	95.5%	-3.0% (-7.5, 1.4)
End of Treatment			
microMITT	83.5%	85.3%	-1.8% (- 8.1, 4.5)
MITT	83.7%	85.4%	-1.7% (-7.1, 3.8)
Clinically Evaluable	89.4%	90.0%	-0.7% (-5.6, 4.3)
Microbiologically Evaluable	88.5%	88.9%	-0.4% (-6.3, 5.4)

Phase 3 Clinical Trial – REASSURE



In July 2022, we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study was designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. In October 2023 we completed enrollment in the REASSURE clinical trial, enrolling 2,222 patients. In January 2024, we announced that ORLYNVAH™ met the primary endpoint of statistical non-inferiority to Augmentin® in the Augmentin®-susceptible population, and demonstrated statistically significant superiority versus Augmentin® in the Augmentin® susceptible population, in the REASSURE clinical trial. A brief overview of the comparator agent, sample size, timing of efficacy assessment and duration of oral dosing is provided in the graphic above. Non-inferiority in this clinical trial is defined by the lower limit of the 95% confidence interval for the treatment difference of no more than -10%.

The table below summarizes the key efficacy data for REASSURE at the TOC visit:

	ORLYNVAH™ 500 mg/500 mg BID N=480 n (%)	Augmentin® (Amoxicillin/clavulanate) 875 mg/125 mg BID N=442 n (%)	Treatment Difference[i] (95% CI)
Overall Response[ii]	296 (61.7)	243 (55.0)	6.7 (**0.3**, 13.0)
Clinical Success[iii]	371 (77.3)	339 (76.7)	0.6 (-4.8, 6.1)
Microbiological Success[iv]	361 (75.2)	295 (66.7)	8.5 (2.6, 14.3)

[i] Difference in oral sulopenem versus Augmentin®; in the m-MITTS population
[ii] Combined clinical and microbiological success (primary endpoint)
[iii] Clinical success at TOC = symptom resolution + no new uUTI symptoms
[iv] Eradication of qualifying uropathogen to $<10^3$ CFU/mL at TOC visit

Safety Profile of ORLYNVAH™ 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 30 years.

In the cIAI trial, among 668 treated patients, treatment-related adverse events were observed in 6.0% and 5.1% of patients on sulopenem and ertapenem, respectively, with the most commonly reported drug-related adverse event being diarrhea, which was observed in 4.5% and 2.4% of patients on sulopenem and ertapenem, respectively. Discontinuations from treatment were uncommon for both regimens, occurring in 1.5% of patients on sulopenem and 2.1% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 7.5% of patients on sulopenem and 3.6% of patients on ertapenem. In the cUTI trial, patients received either sulopenem followed by ORLYNVAH™, if eligible for oral therapy, or ertapenem IV followed by ciprofloxacin or amoxicillin-clavulanate, if eligible for oral therapy. Among 1,392 treated patients, treatment-related adverse events were observed in 6.0% and 9.2% of patients on sulopenem and ertapenem, respectively, with the most commonly reported adverse events being headache (3.0% and 2.2%), diarrhea (2.7% and 3.0%) and nausea (1.3% and 1.6%), on sulopenem and ertapenem, respectively. Discontinuations from treatment were uncommon for both regimens, occurring in 0.4% of patients on sulopenem and 0.6% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 2.0% of patients on sulopenem and 0.9% of patients on ertapenem. In the uUTI trial (SURE 1), patients received either ORLYNVAH™ or ciprofloxacin. Among 1,660 treated patients, treatment related adverse events were observed in 17.0% and 6.2% of patients on sulopenem and ciprofloxacin, respectively. The most commonly reported adverse events were diarrhea (12.4% and 2.5%), nausea (3.7% and 3.6%), and headache (2.2% and 2.2%), for ORLYNVAH™, and ciprofloxacin patients, respectively. The difference in adverse events was driven by diarrhea which, in the majority of patients, was mild and self-limited. Overall discontinuations due to adverse events were uncommon on both regimens and were seen in 1.6% of patients on ORLYNVAH™ and 1.0% of patients on ciprofloxacin. Serious adverse events were seen in 0.7% of patients on ORLYNVAH™, with one drug-related serious adverse event due to transient angioedema, and 0.2% of patients on ciprofloxacin with no drug-related serious adverse event. In the recently completed uUTI trial, REASSURE, patients received either ORLYNVAH™ or Augmentin®. Among 2,214 treated patients, treatment related adverse events were observed in 18.9% and 12.3% of patients on ORLYNVAH™ and Augmentin®, respectively. The most commonly reported adverse events were diarrhea (8.1% and 4.1%), nausea (4.3% and 2.9%), and headache (2.2% and 1.5%), for ORLYNVAH™ and Augmentin® patients, respectively. The difference in adverse events was driven by diarrhea which, in the majority of patients, was mild and self-limited. Overall discontinuations due to adverse events were uncommon on both regimens and were seen in 0.7% of patients on ORLYNVAH™ and 0.4% of patients on Augmentin®. Serious adverse events were seen in 0.0% of patients on ORLYNVAH™ and 0.5% of patients on Augmentin® with no drug-related serious adverse event.

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

Pfizer License Agreement

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

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

Under the Pfizer License, we have paid Pfizer a one-time nonrefundable upfront fee of $5.0 million, a total of $15.0 million in clinical milestones based on first patient dosed in our Phase 3 clinical trials with sulopenem etzadroxil and sulopenem IV. Upon approval of oral sulopenem for commercial sale in the United States by the FDA, we agreed to make a regulatory milestone payment of $20.0 million to Pfizer. In accordance with the Pfizer License, we had the option to deliver notice of our election to defer such payment for up to two years from the date of such approval and a promissory note in the amount of $20.0 million to Pfizer within 30 calendar days of such approval. We delivered the notice and a promissory note to Pfizer in the amount of $20.0 million on October 28, 2024. The note accrues interest at an annual rate of eight percent on a daily compounded basis until paid in full.

We are obligated to pay Pfizer additional milestone payments upon the achievement of other specified regulatory milestones 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 also obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage of marginal net sales of each licensed product. Pfizer also received 381,922 of our Series A preferred shares (which converted to 25,461 ordinary shares in connection with our initial public offering) at a value of $15.71 per share as additional payment for the licensed rights. In addition, if we sublicense or assign any of our rights to any licensed products to a third party, and we receive in connection with such transaction a threshold amount of at least a low nine figure dollar amount over a specified period of time, we will be obligated to pay Pfizer an additional one-time payment of a low eight figure dollar amount.

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

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

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining rights in patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture and any other inventions that are commercially important to the development of our business.

We own four U.S. patents, one Japanese patent, one Korean patent and one Australian patent, with one U.S. patent, the Japanese patent, the Korean patent and the Australian patent directed to the composition of the bilayer tablet of oral sulopenem and its related preparations and/or uses. Two U.S. patents are directed to the method of use of oral sulopenem in treating multiple diseases, including uUTIs. One U.S. patent is directed to the method of use of sulopenem etzadroxil, probenecid, and valproic acid in treating multiple diseases. The patents owned by us are scheduled to expire between 2039 and 2041, excluding any additional term for patent adjustments or patent term extensions. We also own three pending U.S. patent applications, and 26 pending foreign patent applications, which collectively cover uses of sulopenem and probenecid and bilayer tablets of sulopenem etzadroxil and probenecid. We were notified that one pending Canadian patent application, which is directed to the bilayer tablet of oral sulopenem and its related preparations and/or uses, was allowed in 2024. This Notice of Allowance concludes the substantive examination of the patent application and will result in the issuance of a Canadian patent after administrative processes are completed. One pending Australian patent application, which is directed to the use of sulopenem etzadroxil and probenecid in treating multiple diseases, including uUTI, was also recently allowed. Any U.S. or foreign patents issuing from the pending applications are projected to expire between 2039 and 2041, excluding any additional term for patent adjustments or patent term extensions. In addition to patents owned by us, we also rely on the Pfizer License for intellectual property rights that are important or necessary for the development of sulopenem etzadroxil and the IV formulation of sulopenem. We do not however license any patent rights that cover the IV formulation of sulopenem and all patent rights covering the compound sulopenem expired prior to us entering into the Pfizer License. We also rely, in some circumstances, on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

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

Intellectual Property Relating to Oral Sulopenem

As of January 31, 2025, we exclusively license from Pfizer two U.S. patents and three foreign patents, including one U.S. patent directed to composition of matter of sulopenem etzadroxil, which is projected to expire in 2029, subject to potential extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Act, to 2034, and three foreign patents related to sulopenem etzadroxil. We own four U.S. patents, one Japanese patent, one Korean patent and one Australian patent, with one U.S. patent, the Japanese patent, the Korean patent and the Australian patent directed to the composition of the bilayer tablet of oral sulopenem and its related preparations and/or uses. Two U.S. patents are directed to the method of use of oral sulopenem in treating multiple diseases, including uUTIs. One U.S. patent is directed to the method of use of sulopenem etzadroxil, probenecid, and valproic acid in treating multiple diseases. The patents owned by us are scheduled to expire between 2039 and 2041, excluding any additional term for patent adjustments or patent term extensions. We also own three pending U.S. patent applications, and 26 pending foreign patent applications, which collectively cover uses of sulopenem and probenecid and bilayer tablets of sulopenem etzadroxil and probenecid. We were notified that one pending Canadian patent application, which is directed to the bilayer tablet of oral sulopenem and its related preparations and/or uses, was allowed in 2024. This Notice of Allowance concludes the substantive examination of the patent application and will result in the issuance of a Canadian patent after administrative processes are completed. One pending Australian patent application, which is directed to the use of sulopenem etzadroxil and probenecid in treating multiple diseases, including uUTI, was also recently allowed. Any U.S. or foreign patents issuing from the pending applications are projected to expire between 2039 and 2041, excluding any additional term for patent adjustments or patent term extensions.

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 ORLYNVAH™, oral sulopenem in additional indications, 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.

There are a variety of available oral therapies marketed for the treatment of multi-drug resistant infections that we expect to compete with ORLYNVAH™ and would compete with oral sulopenem in additional indications, such as levofloxacin, ciprofloxacin, nitrofurantoin, fosfomycin, amoxicillin-clavulanate, cephalexin, trimethoprim-sulfamethoxazole and pivmecillinam. ORLYNVAH™ could also compete with a few oral antibiotics currently in late-stage clinical development to treat uUTIs, including gepotidacin from GlaxoSmithKline.

We believe that ORLYNVAH™ could compete effectively against these compounds on the basis of ORLYNVAH™'s potential:

•broad range of activity against a wide variety of resistant and MDR gram-negative bacteria;

•low probability of drug resistance;

•favorable safety and tolerability profile;

•convenient oral dosing regimen and opportunity to step down from IV-administered therapy; and

•use as a monotherapy treatment for resistant and MDR gram-negative infections.

There are several IV-administered products marketed for the treatment of infections resistant to first-line therapy for gram-negative infections, including Avycaz from AbbVie Inc. and Pfizer, Vabomere from Melinta Therapeutics, Inc., Zerbaxa from Merck & Co., Zemdri from Cipla Limited, Xerava from Innoviva, Inc, Recarbrio from Merck & Co, and Fetroja from Shionogi & Co., Ltd.

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 ORLYNVAH™;

•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.

QIDP Status

As noted above, the FDA has designated sulopenem and oral sulopenem as QIDPs for the indications of uUTI, cUTI and cIAI as well as community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. QIDP status makes sulopenem eligible to benefit from certain incentives for the development of new antibiotics provided under the GAIN Act. Further, QIDP status could add five years to any other regulatory exclusivity period that may be granted. For example, in October, 2024, the FDA confirmed that an additional five years of marketing exclusivity under the GAIN Act will be added to the regulatory exclusivity granted upon approval of ORLYNVAH™, resulting in a total of ten years marketing exclusivity. QIDP status for other indications is also possible given the coverage of gram-negative and gram-positive bacteria by sulopenem, pending submission of additional documentation and acceptance by the FDA. Fast track status provides an opportunity for more frequent meetings with the FDA, more frequent written communication related to the clinical trials, eligibility for accelerated approval and priority review and the potential for a rolling review.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the EU, extensively regulate, among other things, the research, development, clinical trials, testing, manufacture, including any manufacturing changes, authorization, pharmacovigilance, adverse event reporting, recalls, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, pricing, reimbursement, 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 and jurisdictions, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources. The regulatory requirements applicable to product development, approval and marketing are subject to change, and regulations and administrative guidance often are revised or reinterpreted by government agencies in ways that may have a significant impact on our business.

United States Government Regulation

In the United States, the FDA regulates drug products 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. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor.

The process required by the FDA before a drug product 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;

•design of a clinical protocol and submission to the FDA of an investigational new drug (IND) application which must become effective before human clinical trials may begin;

•approval by an independent institutional review board (IRB) at each clinical site before each trial may be initiated;

•performance of adequate and well-controlled human clinical trials in accordance with good clinical practices (GCPs) to establish the safety and efficacy of the proposed drug product for each indication;

•submission to the FDA of an NDA;

•satisfactory completion of an FDA advisory committee review, if applicable;

•satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices (cGMP), and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;

•satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of clinical data;

•payment of user fees pursuant to the PDUFA;

•securing FDA review and approval of the NDA authorizing marketing of the new drug product for particular indications in the U.S.; and

•commitment to comply with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy (REMS) and the potential requirement to conduct post-approval studies.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. Preclinical tests intended for submission to the FDA to support the safety of a product candidate must be conducted in compliance with GLP regulations and the United States Department of Agriculture's Animal Welfare Act. A drug sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Such studies are typically referred to as IND-enabling studies. Some preclinical testing may continue even after the IND is submitted. With passage of the FDA's Modernization Act 2.0 in December 2022, Congress eliminated provisions in both the FDCA and the Public Health Service Act (PHSA) that required animal testing in support of an NDA or BLA. While animal testing may still be conducted, the FDA was authorized to rely on alternative non-clinical tests, including cell-based assays, microphysiological systems, or bioprinted or computer models.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. 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. Beyond reviewing an IND to assure the safety and rights of patients, the FDA's review also focuses on the quality of the investigation and whether it will be adequate to permit an evaluation of the drug's effectiveness and safety. If there are any outstanding questions, the IND sponsor and the FDA must resolve them before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

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

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must continue to review and reapprove the study at least annually. The IRB, which must operate in compliance with FDA regulations, must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects and must monitor the trial until completed. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data monitoring committee (DMC). This group provides authorization as to whether or not a trial may move forward at designated checkpoints based on review of available data from the study, to which only the DMC maintains access. Suspension or termination of development during any phase of a clinical trial can occur if the DMC determines that the participants or patients are being exposed to an unacceptable health risk or for other reasons.

Clinical Trials

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

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.

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such trials, typically referred to as post-approval clinical trials, may be conducted after initial marketing approval. Moreover, a clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA.

In December 2022, with the passage of the Food and Drug Omnibus Reform Act (FDORA), Congress required sponsors to develop and submit a diversity action plan (DAP) for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, action plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. This action raises questions about the applicability of statutory obligations to submit DAPs and the agency's current thinking on best practices for clinical development.

In June 2023, the FDA issued draft guidance with updated recommendations for GCPs aimed at modernizing the design and conduct of trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The draft guidance is adopted from the International Council for Harmonisation's (ICH) recently updated E6(R3) draft guideline that was developed to enable the incorporation of rapidly developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued draft guidance outlining recommendations for the implementation of decentralized clinical trials.

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.

Clinical Studies Outside the United States in Support of FDA Approval

In connection with our clinical development program, we may conduct trials at sites outside the United States. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee, or IEC, and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

The acceptance by the FDA of study data from clinical trials conducted outside the United States in support of US approval may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted.

Reporting Clinical Trial Results

Under the PHSA, sponsors of clinical trials of certain FDA-regulated products, including prescription drugs and biologics, are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health (the NIH). In particular, information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017.

The PHSA grants the Secretary of Health and Human Services the authority to issue a notice of noncompliance to a responsible party for failure to submit clinical trial information as required. The responsible party, however, is allowed 30 days to correct the noncompliance and submit the required information. As of December 19, 2024, the FDA has issued six notices of non-compliance, thereby signaling the government's willingness to begin enforcing these requirements against non-compliant clinical trial sponsors. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinicaltrials.gov is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. Violations may also result in injunctions and/or criminal prosecution or disqualification from federal grants.

Interactions with FDA during the clinical development program

Following the clearance of an IND and the commencement of clinical trials, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Specifically, sponsors may meet with the FDA prior to the submission of an IND (Pre-IND meeting), at the end of Phase 2 clinical trial (EOP2 meeting) and before a biologics license application (BLA) is submitted (Pre-BLA meeting). Meetings at other times may also be requested. There are five types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-BLA meetings, as well as end of phase meetings such as EOP2 meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product, including for example meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use. A Type D meeting is focused on a narrow set of issues, which should be limited to no more than two focused topics, and should not require input from more than three disciplines or divisions. Finally, INTERACT meetings are intended for novel products and development programs that present unique challenges in the early development of an investigational product. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Expanded Access to an Investigational Drug for Treatment Use

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

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, or Cures Act, passed in 2016, sponsors are required to make policies for evaluating and responding to requests for expanded access for patients publicly available upon the earlier of initiation of a Phase 2 or Phase 3 clinical trial, or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

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

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, a biologics license application or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product 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. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the sponsor, 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. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The law requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. The FDA maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has taken steps to limit what it considers abuse of this statutory exemption in PREA. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

Manufacturing and other regulatory requirements

Concurrent with clinical trials, sponsors usually complete additional animal safety studies, develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing commercial quantities of the product candidate in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other criteria, the sponsor must develop methods for testing the identity, strength, quality, and purity of the finished product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Specifically, the FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Manufacturers and other entities involved in the manufacture and distribution of approved pharmaceuticals are required to register their establishments with the FDA and some state agencies, and they are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other requirements. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture,

preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated. Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product.

Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. The manufacturing facilities may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. If a manufacturing facility is not in substantial compliance with the applicable regulations and requirements imposed when the product was approved, regulatory enforcement action may be taken, which may include a warning letter or an injunction against shipment of products from the facility and/or recall of products previously shipped.

Submission and Review of an NDA

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 CMC and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2025 is $4,310,002 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2025 is $403,889. Under the 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. The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission. Despite these review goals, it is not uncommon for FDA review of an application to extend beyond the PDUFA goal date.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit its filing and substantive review. In pertinent part, the FDA's regulations state that an application "shall not be considered as filed until all pertinent information and data have been received" by the FDA. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the sponsor. The FDA may request additional information rather than accept an application for filing. In this event, the application must be resubmitted with the additional information, and it will also be 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.

In connection with its review of 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. With passage of FDORA, Congress clarified the FDA's authority to conduct inspections by expressly permitting inspections of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to the FDA as well as other persons holding study records or involved in the study process.

Moreover, the FDA will review a sponsor's financial relationship with the principal investigators who conducted the clinical trials in support of the NDA. That is because, under certain circumstances, principal investigators at a clinical trial site may also serve as scientific advisors or consultants to a sponsor and receive compensation in connection with such services. Depending on the level of that compensation and any other financial interest a principal investigator may have in a sponsor, the sponsor may be required to report these relationships to the FDA. The FDA will then evaluate that financial relationship and determine whether it creates a conflict of interest or otherwise affects the interpretation of the trial or the integrity of the data generated at the principal investigator's clinical trial site. If so, the FDA may exclude data from the clinical trial site in connection with its determination of safety and efficacy of the investigational product.

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.

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.

Decisions on an NDA

The FDA reviews an application to determine whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. Ultimately, the FDA will determine whether the expected benefits of the drug product outweigh its potential risks to patients. This assessment is informed by the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks.

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 will issue either a Complete Response Letter (CRL), or an approval letter. A CRL generally contains a statement of specific conditions that must be met before the NDA may be resubmitted and may require additional clinical or preclinical testing in order for FDA to reconsider the application. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. For those seeking to challenge the FDA's CRL decision, the agency has indicated that sponsors may request a formal hearing on the CRL or they may file a request for reconsideration or a request for a formal dispute resolution.

An approval letter, on the other hand, authorizes commercial marketing of the product 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, post-approval 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. 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. In addition, none of these expedited programs changes the standards for approval but they may help expedite the development or approval process of product candidates.

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. 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 meant to treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. These six and ten month review periods are measured from the "filing" date for NDAs for new molecular entities. The FDA will automatically give a priority review designation for the first application submitted in respect of a product for which a QIDP designation was granted.

Limited Population Drug Pathway

With passage of the Cures Act, Congress also authorized the FDA to approve an antibacterial or antifungal drug product, alone or in combination with one or more other drugs, as a "limited population drug." To qualify for this approval, or LPAD, pathway, the drug product must be intended to treat a serious or life-threatening infection in a limited population of patients with unmet needs; the standards for approval of drugs under the FDCA must be satisfied; and FDA must receive a written request from the sponsor to approve the drug as a limited population drug pursuant to this provision. The FDA's determination of safety and effectiveness for such a product must reflect the benefit-risk profile of such drug in the intended limited population, taking into account the severity, rarity, or prevalence of the infection the drug is intended to treat and the availability or lack of alternative treatment in such a limited population. Accordingly, the FDA expects that development programs for drugs eligible for approval under the LPAD pathway will follow streamlined approaches to clinical development such as smaller, shorter or fewer clinical trials.

Any drug product approved under this pathway must be labeled with the statement "Limited Population" in a prominent manner and adjacent to the proprietary name of the drug product. The prescribing information must also state that the drug is indicated for use in a limited and specific population of patients and copies of all promotional materials relating to the drug must be submitted to the FDA at least 30 days prior to dissemination of the materials. If the FDA subsequently approves the drug for a broader indication, the agency may remove any post-marketing conditions applicable to the product, including requirements with respect to labeling and review of promotional materials. Nothing in this pathway to approval of a limited population drug prevents sponsors of such products from seeking designation or approval under other provisions of the FDCA, such as accelerated approval.

Post-Approval Requirements

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

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including post-approval clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. For example, in addition to reporting of adverse reactions to ORLYNVAH™, post marketing requirements for ORLYNVAH™ also include conducting a U.S. surveillance study over a five-year period after the introduction of ORLYNVAH™ to the market to determine if resistance or decreased susceptibility to ORLYNVAH™ is occurring in the target population of bacteria identified in the approved label for ORLYNVAH™.

In addition, 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. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

If a company is found to have promoted off-label uses, it may become subject to administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes products, as well as adverse public relations and reputational harm. The federal government has levied large civil and criminal fines against companies for

alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. Moreover, with passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. In addition, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use. This guidance was finalized by the FDA in January 2025.

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. For example, 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 a variety of federal and state laws. The Prescription Drug Marketing Act (PDMA) was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. In November 2013, the federal Drug Supply Chain Security Act (DSCSA) became effective in the United States, mandating an industry-wide, electronic, interoperable system to trace prescription drugs through the pharmaceutical distribution supply chain with a ten-year phase-in process. Manufacturers were required by November 2023 to have such systems and processes. So as not to disrupt supply chains, the FDA has granted certain exemptions from enhanced drug distribution security requirements for eligible trading partners for particular periods of time.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and effectiveness of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the sponsor to rely, in part, on the FDA's previous findings of safety and effectiveness for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the sponsor. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the Section 505(b)(2) sponsor can establish that reliance on the FDA's previous approval is scientifically appropriate, the sponsor may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support

the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) sponsor.

Exclusivity and Approval of Competing Products

Hatch-Waxman Exclusivity

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA. To obtain approval of a generic drug, a sponsor must submit an abbreviated new drug application (ANDA) to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing conducted for a drug product previously approved under an NDA, known as the reference listed drug (RLD). In addition, Congress authorized the FDA to approve a 505(b)(2) NDA for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

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 sponsor 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. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. 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 data 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.

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. In October 2024, the FDA confirmed that an additional five years of marketing exclusivity under the GAIN Act will be added to the regulatory exclusivity granted upon approval of ORLYNVAH™, resulting in a total of ten years marketing exclusivity. This extension is in addition to any pediatric exclusivity extension awarded, and the extension will be awarded only to a drug first approved on or after the date of enactment.

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

Pediatric Exclusivity

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

regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the period during which the FDA cannot approve another application.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of the IND and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Federal and state data privacy laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), the Department of Health and Human Services (HHS) has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them. Our clinical trials are regulated by the Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

At the state level, California has enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA went into effect on January 1, 2020 and requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. Additionally, effective starting on January 1, 2023, the California Privacy Rights Act, or CPRA, significantly modified the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. The CCPA and CPRA could impact our business activities depending on how it is interpreted and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and individually identifiable health information. These provisions may apply to some of our business activities.

In addition to California, at least eighteen other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2024 legislative sessions that will go into effect in 2025 and beyond. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, the State of Washington passed the My Health My Data Act in 2023 which specifically regulated health information that is not otherwise regulated by the HIPAA rules, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation in 2024. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their

use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act.

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.

Non-clinical Studies

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with GLP principles as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies, both *in vitro* and *in vivo*, must be planned, performed, monitored, recorded, reported and archived in accordance with GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical Trials

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 (CTR) became effective in the EU and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one EU Member State will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

Beyond streamlining the process, the new regulation includes a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors, and a harmonized procedure for the assessment of applications for clinical trials, which is divided into two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the European Union at the EU Clinical Trials Registry (https://eudract.ema.europa.eu).

Marketing Authorization

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. Pursuant to Regulation (EC) No. 726/2004, 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, a sponsor 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.

Within this framework, manufacturers may seek approval of hybrid medicinal products under Article 10(3) of Directive 2001/83/EC. Hybrid applications rely, in part, on information and data from a reference product and new data from appropriate preclinical tests and clinical trials. Such applications are necessary when the proposed product does not meet the strict definition of a generic medicinal product, or bioavailability studies cannot be used to demonstrate bioequivalence, or there are changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration of the generic product compared to the reference medicinal product. In such cases the results of tests and trials must be consistent with the data content standards required in the Annex to the Directive 2001/83/EC, as amended by Directive 2003/63/EC.

Hybrid medicinal product applications have automatic access to the centralized procedure when the reference product was authorized for marketing via that procedure. Where the reference product was authorized via the decentralized procedure, a hybrid application may be accepted for consideration under the centralized procedure if the sponsor shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation, or the granting of a single marketing authorization for the medicinal product is in the interest of patients in the EU.

Conditional Marketing Authorization

In particular circumstances, EU legislation (Article 14–a Regulation (EC) No 726/2004 (as amended by Regulation (EU) 2019/5 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables sponsors to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full MA. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the product candidate is intended for the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening diseases; (2) the product candidate is intended to meet unmet medical needs of patients; (3) the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required; (4) the risk-benefit balance of the product candidate is positive, and (5) it is likely that the sponsor will be in a position to provide the required comprehensive clinical trial data. A conditional MA may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new clinical trials and with respect to the collection of pharmacovigilance data. Conditional MAs are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional MA.

Exceptional Circumstances

A MA may also be granted "under exceptional circumstances" under Article 14(8) of Regulation (EC) No 726/2004 when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable. Under these procedures, before granting the MA, the EMA or the competent authorities of the European Union Member States make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Regulatory requirements after marketing authorization

As in the United States, both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations. The holder of an EU marketing authorization for a medicinal product must, for example, comply with EU pharmacovigilance legislation and its related regulations and guidelines which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. The

manufacturing process for medicinal products in the European Union is also highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, including compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients.

In the European Union, the advertising and promotion of approved products are subject to EU Member States' laws governing promotion of medicinal products, interactions with clinicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion, which is prohibited in the European Union.

Regulatory Data Protection

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. Data exclusivity prevents sponsors for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company can complete a full MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

In this context, it should be noted that the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products was published in April 2023 and includes, among other things, provisions that would potentially reduce the duration of regulatory data protection. The European Parliament requested several amendments in April 2024. At this time, the proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry in the long term, if and when adopted.

Reimbursement and pricing of prescription pharmaceuticals

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Member States may approve a specific price for a product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Brexit and the Regulatory Framework in the United Kingdom

The U.K.'s withdrawal from the EU, commonly referred to as Brexit, took place on January 31, 2020. The EU and the UK reached an agreement on their new partnership in the Trade and Cooperation Agreement, which entered into force on May 1, 2021. As of January 1, 2021, the Medicines and Healthcare Products Regulatory Agency (the MHRA) became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern

Ireland continues to be subject to EU rules under the Northern Ireland Protocol, as amended by the so called Windsor Framework agreed in February 2023. As of January 1, 2025, the changes introduced by the Windsor Framework resulted in the MHRA being responsible for approving all medicinal products destined for the United Kingdom market (Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. The MHRA relies on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended) (the HMR) as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the U.K.'s withdrawal from the EU.

As of January 1, 2024 on, a new international recognition procedure (IRP) applies which intends to facilitate approval of pharmaceutical products in the U.K. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators (RRs). The RRs notably include EMA and regulators in the EEA member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.).The RR assessment must have undergone a full and standalone review. RR assessments based on reliance or recognition cannot be used to support an IRP application. A CHMP positive opinion or an MRDC positive end of procedure outcome is an RR authorization for the purposes of IRP.

General Data Protection Regulation

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

In July 2020, the Court of Justice of the European Union (CJEU) invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. Following the CJEU decision, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-US Privacy Shield. The European Commission initiated the process to adopt an adequacy decision for the EU-US Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business at the international level.

On June 23, 2016, the electorate in the United Kingdom (U.K.) voted in favor of leaving the EU, commonly referred to as Brexit. As with other issues related to Brexit, there are open questions about how personal data will be protected in the U.K. and whether personal information can transfer from the EU to the U.K. Following the withdrawal of the U.K. from the EU, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by GDPR. While the Data Protection Act of 2018 in the U.K. that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the U.K., it is unclear whether transfer of data from the EEA to the U.K. will remain lawful under the GDPR, although these transfers currently are permitted by an adequacy decision from the European Commission. The U.K. government has already determined that it considers all European Union 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the U.K. to the EU/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the U.K. as being "essentially adequate" for purposes of data transfer from the EU to the U.K., although this decision may be re-evaluated in the future. The U.K. and the U.S. have also agreed to a U.S.-U.K. "Data Bridge," which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the U.K. to the United States. In addition to the U.K., Switzerland is also in the process of approving an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data

Privacy Framework and the U.S.-U.K. Data Bridge in relation to data transfers from Switzerland to the United States). Any changes or updates to these developments have the potential to impact our business.

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; the federal false claims and civil monetary penalty laws, including the federal False Claims Act; HIPAA; HIPAA, as amended by the Health Information Technology and Clinical Health Act of 2009, and its implementing regulations; the federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act," and its implementing regulations; and state and foreign law equivalents of each of the aforementioned federal laws, such as anti-kickback and false claims laws.

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.

In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for drug products under government health care programs. Other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief, and Economic Security Act.

The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our

product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Under current legislation, the actual reductions in Medicare payments may vary up to 4%. The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriations Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017 (TCJA), Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the PPACA brought by several states without specifically ruling on the constitutionality of the PPACA. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, Centers for Medicare and Medicaid Services (CMS) issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program (SIP), to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America (PhRMA), but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Seven states (Colorado, Florida, Maine, New Hampshire, New Mexico, Texas and Vermont) have passed laws allowing for the importation of products from Canada. North Dakota and Virginia have passed legislation establishing workgroups to examine the impact of a state importation program. As of May 2024, five states (Colorado, Florida, Maine, New Hampshire and New Mexico) had submitted Section 804 Importation Program proposals to the FDA. On January 5, 2023, the FDA approved Florida's plan for Canadian product importation. That state now has authority to import certain products from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each product selected for importation, which must be approved by the FDA. The state will also need to relabel the products and perform quality testing of the products to meet FDA standards.

Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. The Inflation Reduction Act of 2022 (IRA), further delayed implementation of this rule to January 1, 2032.

On August 16, 2022, the IRA was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare beginning in 2026, with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation first due in 2023; and replaces the Part D coverage gap discount program with a new discounting program beginning in 2025. The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in

2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least nine years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. On October 2, 2024, in final guidance, CMS indicated that it would announce the selection of up to 15 additional drugs covered by Part D for the second cycle of negotiations by February 1, 2025. That announcement was made on January 17, 2025. This second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027.

On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce (Chamber), Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, and wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional health care organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Commercialization Strategy and Organization

After receiving positive data from our REASSURE trial, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing stakeholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Since we may not ultimately pursue or consummate a strategic transaction, we have begun to evaluate other options for maximizing the value of ORLYNVAH™, which may include seeking raising capital to support the commercialization of ORLYNVAH™.

We have not yet established a commercial organization or distribution capabilities for ORLYNVAH™. In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may commercialize ORLYNVAH™ in the United States with a commercial partner and/or on our own with a targeted sales force in the community setting.

Subject to the outcome of our strategic process and our ability to raise sufficient capital, we may, directly or through a commercial partner, plan to build an awareness program to familiarize physicians in the community setting with the rising rate of resistance of pathogens to the current oral therapies for uUTI, and in particular, the resistance rate of *E. coli* to quinolones in the specific areas those physicians are practicing. Additionally, subject to the outcome of our strategic process and our ability to raise sufficient capital, we may, directly or through a commercial partner, plan to develop marketing, sales and training materials as well as begin interacting with physicians to discuss the uUTI disease state and challenges that the existing treatments are facing.

Subject to the outcome of our strategic process and our ability to raise sufficient capital, we may, directly or through a commercial partner, plan to build a commercial infrastructure to launch ORLYNVAH™ in the United States. We expect that any commercial infrastructure would be led operationally by highly experienced management personnel and would be comprised of a sales force, marketing team, health resource group and a managed markets group focused on reimbursement and access with third-party

payors. We expect that any commercialization plan would include a patient and healthcare practitioner support group to assist with information requests, reimbursement logistics and assistance, and provide educational materials where appropriate.

In the event we were to build a commercial infrastructure ourselves, we would expect our sales team would focus its efforts on the physicians in the community and we would plan to segment these physicians into priority targets based on three key variables: the rate of resistance in a physician's territory, the number of prescriptions generated by an individual physician for uUTI and the commercial payor coverage in that territory. With these target physicians, we would plan to deploy our commercial resources to highlight the patient profiles that would be appropriate for ORLYNVAH™, including patients with suspected or known quinolone resistant pathogens. We expect our commercial teams would work with physicians in the infectious disease field to answer questions regarding ORLYNVAH™ and its clinical results and its pharmacokinetic profile, conduct medical education events regarding the emerging science and build awareness of sulopenem. To the extent access for, and awareness of, our sulopenem program was to increase, 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.

In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we would likely focus 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 a potential 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 have relied on a small number of third-party contract manufacturers for all of our required raw materials, drug substance, and finished drug product for our preclinical research and clinical trials and will continue to do so should we proceed to build a commercial infrastructure to launch ORLYNVAH™ in the United States. As of January 31, 2025, we had a 3-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 one supplier for sulopenem etzadroxil API, with each supplier capable of producing commercial scale quantities under cGMP conditions. We also have a third-party manufacturer that is able to produce the ORLYNVAH™ bilayer tablets. Given the importance of ORLYNVAH™ to our potential commercial results, we will consider establishing additional sources in the future if we pursue commercializing ORLYNVAH™ in the United States.

Employees and Human Capital

As of January 31, 2025, we had nine full-time employees, including a total of two employees with M.D. or Ph.D. degrees. We are also supported by consultants and contractors in most areas of the business, including clinical, regulatory, CMC, Quality Assurance and finance and business and operations support. Three of our employees are 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. We may need to increase our workforce to support commercialization activities, and, if we pursue additional clinical work related to other indications, we may increase our research and development headcount.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing employees and additional employees that may be hired. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of share-based compensation awards.

Our Corporate Information

We were incorporated under the laws of the Republic of Ireland in June 2015 as a limited company and re-registered as a public limited company on March 20, 2018. Our executive offices are located at 3 Dublin Landings, North Wall Quay, Dublin 1, D01 C4E0, Ireland, and our telephone number is (+353) 1 903 8354.

Available Information

We maintain a website with the address www.iterumtx.com. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934 (the Exchange Act). We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. You can review our electronically filed reports, proxy and information statements and other information that we file with the SEC on the SEC's web site at www.sec.gov. We also make available, free of charge on our website, the reports filed with the SEC

by our executive officers, directors and 10% shareholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K.

Item 1A. Risk Factors.

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

Risks Related to Our Evaluation of Strategic Options

Our exploration and pursuit of strategic alternatives may not be successful.

Our board of directors, after receiving positive data from our REASSURE clinical trial in January 2024, determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing stakeholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Following receipt of U.S. Food and Drug Administration (FDA) approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized.

Despite our plan to devote significant efforts to identify and evaluate potential strategic options, the process may not result in any definitive offer to consummate such a transaction, or, if we receive such a definitive offer, the terms may not be as favorable as anticipated or may not result in the execution or approval of a definitive agreement. Even if we enter into a definitive agreement, we may not be successful in completing a transaction or, if we complete such a transaction, it may not enhance shareholder value or deliver expected benefits. Since we may not ultimately pursue or consummate a strategic transaction, we have begun to evaluate other options for maximizing the value of ORLYNVAH™, which may include seeking to raise capital to support the commercialization of ORLYNVAH™.

In the event that we do not successfully identify a viable strategic option or, consummate such a transaction, or if we are unable to raise sufficient capital to fund our operations and commercialize ORLYNVAH™, our board of directors may determine that a liquidation and dissolution of our business approved by shareholders is the best method to seek to maximize shareholder value.

In the event that we do not successfully identify a viable strategic option or, consummate such a transaction, or if we are unable to raise sufficient capital to fund our operations and commercialize ORLYNVAH™, our board of directors may determine that a liquidation and dissolution of our business approved by shareholders is the best method to seek to maximize shareholder value. In such an event, the amount of cash available for distribution to our shareholders, if any, will depend heavily on the timing of such liquidation as well as the amount of cash that will need to be reserved for commitments and contingent liabilities.

There can be no assurance that the process to identify a strategic alternative for our business will result in a successfully consummated transaction. If we are unable to identify a viable strategic option or if such a transaction is not completed in a timely manner, or if we are unable to raise sufficient capital to fund our operations and commercialize ORLYNVAH™, our board of directors may determine that a liquidation and dissolution of our business approved by shareholders is the best method to seek to maximize stakeholder value. In such an event, the amount of cash available for distribution to our shareholders, if any, will depend heavily on the timing of such decision and, ultimately, such liquidation, since the amount of cash available for distribution continues to decrease as we fund our operations while we evaluate our strategic options.

In addition, if our board of directors were to approve and recommend, and our shareholders were to approve, a dissolution and liquidation of our business, we would be required under Irish company law (in addition to paying the costs of the liquidation) to pay our outstanding obligations, including amounts owed to Pfizer Inc. (Pfizer), as well as to make reasonable provisions for contingent and unknown obligations, prior to making any distributions in liquidation to our shareholders. As a result of this requirement, a portion of our assets may need to be reserved pending the satisfaction of such obligations. In addition, we may be subject to litigation or other claims related to a liquidation and dissolution of our business. If a liquidation and dissolution are pursued, our board of directors, in consultation with its legal and financial advisors, would need to evaluate these matters and make a determination about a reasonable amount to reserve.

Accordingly, holders of our ordinary shares and other securities could lose all or a significant portion of their investment in the event of a liquidation and dissolution of our company.

Risks Related to Our Financial Position and Capital Requirements

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

We may be forced to delay or reduce the scope of our development programs, commercialization activities and/or limit or cease our operations if we are unable to obtain additional funding to support our current operating plan. We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of December 31, 2024, we had $24.1 million of

cash and cash equivalents. Subsequently, we have paid off debt and sold additional ordinary shares under the "at the market offering" agreement (the Sales Agreement), entered into on October 7, 2022, with H.C. Wainwright & Co. LLC (HC Wainwright), as agent, pursuant to which we may offer and sell our ordinary shares for aggregate gross proceeds of up to $25.0 million, from time to time through HC Wainwright by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended (the Securities Act). Based on our available cash resources, we do not believe that our existing cash and cash equivalents, will enable us to fund our operating expenses for the next 12 months from the date of filing this Annual Report on Form 10-K.

This condition raises substantial doubt about our ability to continue as a going concern within one year after the date the financial statements included elsewhere in this Annual Report on Form 10-K are issued. Management's plans in this regard are described in Note 1 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K. However, although Management intends to pursue plans to obtain additional funding to finance its operations, and the Company has successfully raised capital in the past, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all. In the event that these plans cannot be effectively realized, there can be no assurance that we will be able to continue as a going concern.

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 have a limited operating history, have not generated any product revenue and have incurred net losses in each year since our inception in 2015. As of December 31, 2024, we had an accumulated deficit of $486.1 million, cash and cash equivalents of $24.1 million. On October 25, 2024, we received approval of our New Drug Application (NDA) by the FDA for ORLYNVAH™ (sulopenem etzadroxil and probenecid) for the treatment of uncomplicated urinary tract infections (uUTIs) caused by the designated microorganisms *Escherichia coli, Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women with limited or no alternative oral antibacterial treatment options.

We have financed our operations to date primarily with the issuance of ordinary shares, nominal value $0.01 per share (the ordinary shares), and convertible preferred shares, pre-funded warrants and warrants, debt raised under a financing arrangement with Silicon Valley Bank (SVB), a sub-award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) program and the proceeds of a private placement which closed in January 2020 (the Private Placement) and a subsequent rights offering (the 2020 Rights Offering) pursuant to which our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), sold units (Units) consisting of (i) 6.500% Exchangeable Senior Subordinated Notes due 2025 (Exchangeable Notes); and (ii) Limited Recourse Royalty-Linked Subordinated Notes (RLNs), to certain existing and new investors. In April 2018, we entered into a secured credit facility with SVB and made an initial drawdown of $15.0 million pursuant to a loan and security agreement. In April 2020, we entered into a note (PPP loan) with SVB of $0.7 million under the Paycheck Protection Program. In early June 2020, we issued and sold, in a registered direct offering (June 3, 2020 Offering), ordinary shares for aggregate gross proceeds to us of $5.0 million and net proceeds of $4.3 million after deducting fees payable to the placement agent and other offering expenses payable by us. In late June 2020, we issued and sold, in a registered direct offering (June 30, 2020 Offering), ordinary shares for aggregate gross proceeds to us of $5.0 million and net proceeds of $4.2 million after deducting fees payable to the placement agent and other offering expenses payable by us. In October 2020, we issued and sold, in a registered public offering (October 2020 Offering), ordinary shares and pre-funded warrants exercisable for ordinary shares, each offered together with warrants exercisable for ordinary shares, for aggregate gross proceeds to us of $17.4 million and net proceeds of $15.5 million after deducting fees payable to the placement agent and other offering expenses payable by us. On February 8 and February 10, 2021, we issued and sold, pursuant to an underwritten agreement and including the underwriter's exercise in full of its option to purchase additional ordinary shares (February 2021 Underwritten Offering), ordinary shares for aggregate gross proceeds to us of $46.0 million and net proceeds of $42.1 million after deducting fees payable to the underwriter and other offering expenses payable by us. On February 12, 2021, we issued and sold, in a registered public offering (February 2021 Registered Direct Offering), ordinary shares for aggregate gross proceeds to us of $35.0 million and net proceeds of $32.2 million after deducting fees payable to the placement agent and other offering expenses payable by us. On October 7, 2022, we entered into the Sales Agreement with HC Wainwright, as agent, pursuant to which we may offer and sell ordinary shares for aggregate gross sales proceeds of up to $16.0 million (subject to the availability of ordinary shares), from time to time through HC Wainwright by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act. On December 10, 2024 we filed a prospectus supplement with the SEC pursuant to which we may offer and sell ordinary shares having an aggregate offering price of up to an additional $25.0 million through HC Wainwright pursuant to the Sales Agreement. In August 2024, we completed a rights offering (the 2024 Rights Offering) in which we sold an aggregate of 12,243,930 non-transferable subscription rights to purchase an aggregate of 6,121,965 units (Units) at a subscription price of $1.21 per whole Unit, consisting of (a) one ordinary share, (b) a warrant to purchase 0.50 ordinary shares, at an exercise price of $1.21 per whole ordinary share from the date of issuance through its expiration one year from the date of issuance and (c) a warrant to purchase one ordinary share, at an exercise price of $1.21 per whole ordinary share from the date of issuance through its expiration five years from the date of issuance. The net proceeds from the 2024 Rights Offering, after deducting dealer-manager fees and other offering expenses payable by us, were $5.4 million. During the year ended December 31, 2024, we sold 10,327,787 ordinary shares under the Sales Agreement at an average price of $1.94 per

share for net proceeds of $19.4 million. As of December 31, 2024, net proceeds of $18.0 million have been received from the exercise of certain warrants issued as part of the June 30, 2020 Offering, October 2020 Offering, February 2021 Underwritten Offering and the 2024 Rights Offering. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical and clinical development, for our sulopenem program. On January 31, 2025, our Exchangeable Notes matured and the aggregate outstanding principal amount of $11.1 million together with accrued and unpaid interest became due. We repaid the aggregate principal and accrued and unpaid interest to noteholders in full on January 31, 2025.

Following receipt of the complete response letter from the FDA in relation to our NDA for oral sulopenem in July 2021 (the CRL), in order to reduce operating expenses and conserve cash resources, we halted any remaining pre-commercial activities for oral sulopenem and limited spending to essential costs required in connection with the resubmission of the NDA. After receiving positive data from our REASSURE clinical trial, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing shareholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Following receipt of FDA approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized. We cannot provide any commitment regarding when or if this strategic process will result in any type of transaction however, and no assurance can be given that we will pursue a potential sale, licensing arrangement or other disposition of our rights to sulopenem. In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we would expect to continue to incur significant expenses and increasing operating losses if we engage a commercial partner and/or seek to directly commercialize ORLYNVAH™, seek marketing approval for other product candidates, if clinical trials are successful, and engage and pursue the development of our sulopenem program in additional indications, including through preclinical and clinical development. Our expenses will also increase substantially if and as we:

- establish sales, marketing and distribution capabilities either directly or through a third-party, to commercialize ORLYNVAH™ in the United States;
- establish sales, marketing and distribution capabilities either directly or through a third-party, to commercialize oral sulopenem in additional indications and/or any future product candidates in the United States, if we obtain marketing approval from the FDA;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of ORLYNVAH™ and undertake commercialization activities;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of oral sulopenem in additional indications and/or any future product candidates, if we obtain marketing approval, and undertake commercialization activities;
- 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;
- acquire or in-license other product candidates or technologies; and
- initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates.

We will require additional capital to fund our operations. If we fail to obtain financing when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing pharmaceutical products is a time-consuming, expensive and uncertain process that takes years to complete. We are now focused on a strategic process to sell, license, or otherwise dispose of our rights to ORLYNVAH™ with the goal of maximizing stakeholder value and engaged a financial advisor to assist management and the board in evaluating strategic alternatives. We cannot provide any commitment regarding when or if this strategic process will result in any type of transaction however, and no assurance can be given that we will determine to pursue a potential sale, licensing arrangement or other disposition of our rights to sulopenem. In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we expect to continue to incur significant expenses and increasing operating losses in connection with our ongoing activities including any expenses that may be incurred in preparation for the commercial launch of ORLYNVAH™.

We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all.

Although we have successfully raised capital in the past, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all.

In the event our strategic process does not result in any type of transaction, we expect that additional capital will be required as we incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution for ORLYNVAH™ if we engage a commercial partner and/or seek to directly commercialize ORLYNVAH™. 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. If we fail to obtain financing when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts, which would have a negative effect on our financial condition and our ability to develop and commercialize our sulopenem program and otherwise pursue our business strategy and we may be unable to continue as a going concern.

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 costs of commercialization activities for ORLYNVAH™ including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the costs of commercialization activities for 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 revenue received from any commercial sales of ORLYNVAH™;
- the receipt of revenue received from any commercial sales of sulopenem and other product candidates, if we receive marketing approval;
- the receipt of marketing approval and revenue received from any potential commercial sales of 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 amount and timing of any payments we may be required to make in connection with the RLNs;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;
- the timing and costs of our clinical trials of our product candidates, including any clinical trials or non-clinical studies which may be required for regulatory approval of our product candidates;
- the timing of regulatory filings;
- the timing of regulatory review and potential approval of any product candidates;
- 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 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 operating as a public company;
- the extent to which we in-license or acquire other products and technologies; and
- the outcome, impact, effects and results of our evaluation of corporate, strategic, financial and financing alternatives, including the terms, timing, structure, value, benefits and costs of any corporate, strategic, financial or financing alternative and our ability to complete one at all.

Our financial statements include substantial non-operating gains or losses resulting from required quarterly revaluation under generally accepted accounting principles of our outstanding derivative instruments.

Generally accepted accounting principles in the United States require that we report the value of certain derivatives in instruments we have issued as liabilities on our balance sheet and report changes in the value of these derivatives as non-operating gains or losses on our statement of operations. The value of the derivatives is required to be recalculated (and resulting non-operating gains or losses reflected in our statement of operations and resulting adjustments to the associated liability amounts reflected on our balance sheet) on a quarterly basis. The valuations are based upon a number of factors and estimates, including estimates based upon management's judgment. Due to the nature of the required calculations, changes in management's assumptions may result in significant changes in the value of the derivatives and resulting gains and losses on our statement of operations.

We are heavily dependent on the success of our sulopenem program, and our ability to successfully commercialize ORLYNVAH™ and to develop, obtain additional marketing approvals for and successfully commercialize oral sulopenem and IV sulopenem. 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 ORLYNVAH™ and sulopenem. Our prospects, including our ability to finance our operations and generate revenue from product sales, currently depend entirely on the development and commercialization of ORLYNVAH™. After receiving positive data from our REASSURE clinical trial in January 2024, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing shareholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Following receipt of FDA approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized. We cannot provide any commitment regarding when or if this strategic process will result in any type of transaction however, and no assurance can be given that we will determine to pursue a potential sale, licensing arrangement or other disposition of our rights to sulopenem.

We do not expect to generate significant revenue unless and until we commercialize ORLYNVAH™ and obtain marketing approval for, and commercialize, oral sulopenem in additional indications. In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Outside of the United States, we continue to evaluate the options to maximize the value of our sulopenem program. 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:

- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate commercial quantities of ORLYNVAH™, and that can support clinical development and provide adequate commercial quantities of sulopenem, if approved;
- establishing sales, marketing and distribution capabilities either directly or through a third-party, to commercialize ORLYNVAH™ and/or sulopenem or entering into collaboration arrangements for the commercialization of ORLYNVAH™ and/or sulopenem where we choose not to commercialize directly ourselves;
- obtaining market acceptance of ORLYNVAH™, and sulopenem, if approved, as viable treatment options;
- enrolling and successfully completing any clinical trials that may be required for regulatory approval of additional product candidates;
- applying for and obtaining marketing approval for IV sulopenem and/or oral sulopenem in additional indications; and
- protecting and maintaining our rights to our intellectual property portfolio related to our sulopenem program;

Because of the numerous risks and uncertainties associated with developing and commercializing 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 such studies or with the development of our sulopenem program or any future product candidates. We anticipate that significant costs will be associated with the commercial launch of ORLYNVAH™ and/or oral sulopenem in additional indications, if approved for commercial sale. Where we enter into collaboration arrangements with third-party collaborators for commercialization of ORLYNVAH™ or other product candidates, our product revenues or the profitability of these product revenues to us would likely be lower than if we were to directly market and sell products in those markets.

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

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

The indenture governing the RLNs (the RLN Indenture) contains affirmative and negative covenants which impose operating and other restrictions on us, including, among other things, transferring any material assets. Moreover, obtaining a consent to a waiver of these terms is subject to a veto right of 30% of the outstanding RLNs, under the RLN Indenture, and must include Sarissa Capital Offshore Master Fund LP, Sarissa Capital Catapult Fund LLC and Sarissa Capital Hawkeye Fund LP (collectively with their affiliates, Sarissa) so long as Sarissa and its affiliates own at least 10% of the outstanding RLNs. This veto right could make it more difficult for us to obtain a waiver than would otherwise be the case.

In addition, the exercise price and the number of shares issuable under our outstanding warrants are subject to adjustment pursuant to the terms of the applicable warrant. This indebtedness could make it more difficult for us to raise additional capital to fund our operations.

We may incur substantially more debt or take other actions that would intensify the risks discussed above.

We and our subsidiaries may be able to incur substantial additional debt in the future, subject to the restrictions contained in our current and future debt instruments, some of which may be secured debt.

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

Unless and until we can generate a substantial amount of revenue from our sulopenem program or future product candidates, we expect to finance our future cash needs through equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements, marketing and distribution arrangements or government funding.

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.

On October 7, 2022, we filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on October 17, 2022 (File No. 333-267795), and pursuant to which we registered for sale up to $100.0 million of any combination of our debt securities, ordinary shares, preferred shares, subscription rights, purchase contracts, units and/or warrants from time to time and at prices and on terms that we may determine. The extent to which we are able to utilize a shelf registration statement as a source of funding will depend on a number of factors, including the prevailing market price of our ordinary shares, general market conditions and applicability, or not, of restrictions on our ability to utilize the shelf registration statement to sell more than one-third of the market value of our public float, meaning the aggregate market value of voting and non-voting ordinary shares held by non-affiliates, in any trailing 12-month period.

On October 7, 2022, we entered into the Sales Agreement with HC Wainwright, as agent, pursuant to which we may offer and sell ordinary shares for aggregate gross sales proceeds of up to $16.0 million (subject to the availability of ordinary shares), from time to time through HC Wainwright by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act. On December 10, 2024 we filed a prospectus supplement with the SEC pursuant to which we may offer and sell ordinary shares having an aggregate offering price of up to an additional $25.0 million through HC Wainwright pursuant to the Sales Agreement.

Our issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our ordinary shares to decline, and our shareholders may not agree with our financing plans or the terms of such financings. To the extent that we raise additional capital through the sale of ordinary shares, convertible securities or other equity securities, the ownership interests of our then existing shareholders may be materially diluted, and the terms of these securities could include liquidation or other preferences and antidilution protections that could adversely affect the rights of our then existing shareholders. Further debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, which could adversely affect our ability to conduct our business. In addition, securing additional financing would require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

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

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

While we received approval for ORLYNVAH™ for the treatment of uUTIs caused by the designated microorganisms *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women who have limited or no alternative oral antibacterial treatment options, due to a variety of factors, including those described in this "Risk Factors" section, we may nonetheless be delayed in obtaining or ultimately be unable to obtain FDA approval for oral sulopenem in additional indications or for any other product or to successfully commercialize ORLYNVAH™.

Because we have limited financial resources, we initially focused our sulopenem development program on the specific indications of uUTI, complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (cIAI), all of which are focused on what we believe to be the most pressing near-term medical needs, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other potential product candidates or developing our sulopenem program in other indications that may prove to have greater commercial potential. For example, while we believe that sulopenem has the potential to treat cIAIs and cUTIs in humans based on the results of prior preclinical studies and clinical trials, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy in our Phase 3 cIAI and cUTI clinical trials. While we believe the secondary supporting analyses and safety data in all three prior Phase 3 clinical trials support the potential of sulopenem in the treatment of multi-drug resistant infections, we cannot guarantee that these supporting analyses are indicative of efficacy of sulopenem in treating cIAIs or cUTIs.

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

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

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

We hold our cash and cash equivalents that we use to meet our working capital and operating expense needs in deposit accounts that could be adversely affected if the financial institutions holding such funds fail.

We hold our cash and cash equivalents that we use to meet our working capital and operating expense needs in deposit accounts at multiple financial institutions. The balance held in these accounts typically exceeds the Federal Deposit Insurance Corporation (FDIC), standard deposit insurance limit or similar government guarantee schemes. If a financial institution in which we hold such funds fails or is subject to significant adverse conditions in the financial or credit markets, we could be subject to a risk of loss of all or a portion of such uninsured funds or be subject to a delay in accessing all or a portion of such uninsured funds. Any such loss or lack of access to these funds could adversely impact our short-term liquidity and ability to meet our operating expense obligations.

For example, on March 10, 2023, Silicon Valley Bank (SVB), and Signature Bank, were closed by state regulators and the FDIC was appointed receiver for each bank. The FDIC created successor bridge banks and all deposits of SVB and Signature Bank were transferred to the bridge banks under a systemic risk exception approved by the United States Department of the Treasury, the Federal Reserve and the FDIC. If financial institutions in which we hold funds for working capital and operating expenses were to fail, we cannot provide any assurances that such governmental agencies would take action to protect our uninsured deposits in a similar manner.

We also maintain investment accounts with other financial institutions in which we hold our investments and, if access to the funds we use for working capital and operating expenses is impaired, we may not be able to open new operating accounts or to sell investments or transfer funds from our investment accounts to new operating accounts on a timely basis sufficient to meet our operating expense obligations.

Risks Related to Product Development and Commercialization

In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Should we seek to commercialize ORLYNVAH™, we are heavily dependent on the success of ORLYNVAH™, which the FDA has approved for the treatment of uUTIs caused by certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options. Any failure to successfully commercialize

ORLYNVAH™ or inability to obtain marketing approval for any other product candidates, or significant delays in doing so, will materially harm our business.

We have invested a significant portion of our efforts and financial resources in the development of ORLYNVAH™. After receiving positive data from our REASSURE clinical trial in January 2024, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing shareholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Following receipt of FDA approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized. We cannot provide any commitment regarding when or if this strategic process will result in any type of transaction however, and no assurance can be given that we will determine to pursue a potential sale, licensing arrangement or other disposition of our rights to sulopenem. In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Outside of the United States, we continue to evaluate the options to maximize the value of our sulopenem program. There remains a significant risk that we may fail to successfully commercialize ORLYNVAH™.

Our ability to generate meaningful product revenues depends heavily on the successful commercialization of ORLYNVAH™ and our obtaining marketing approval for oral sulopenem in additional indications and other product candidates. The success of ORLYNVAH™ and, any other approved products, will depend on a number of factors, including the following:

- establishing and maintaining arrangements with third-party manufacturers for commercial supply and receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities from applicable regulatory authorities;
- receiving marketing approval from the FDA and/or other comparable foreign regulatory authority for IV sulopenem, oral sulopenem in additional indications and/or other product candidates;
- maintaining an effective sales and marketing organization to successfully generate recurring sales of ORLYNVAH™;
- receiving acceptance of ORLYNVAH™ by patients, the medical community and third-party payors, including hospital formularies;
- achieving approval of favorable prescribing information;
- effectively competing with other therapies;
- maintaining a continued acceptable safety profile of ORLYNVAH™;
- securing contracts to allow ORLYNVAH™ to be paid for by private and public health insurance plans;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting our rights in our intellectual property portfolio; and
- obtaining and maintaining adequate distribution levels of ORLYNVAH™ at all appropriate trade channels.

Successful development of ORLYNVAH™ and sulopenem for the treatment of additional indications, if any, or for use in other patient populations and our ability to broaden the label for ORLYNVAH™ will depend on similar factors. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize ORLYNVAH™ for uUTI or for any other indication, which would materially harm our business.

If clinical trials of 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 sulopenem or any other product candidate.

While we received marketing approval from the FDA for ORLYNVAH™ for the treatment of uUTIs caused by the certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment option, we may not commercialize, market, promote, or sell ORLYNVAH™ for any additional indications or any other 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. While we received an approval for ORLYNVAH™ from the FDA in October 2024, we have not submitted an NDA to the FDA for any of our other product candidates or any similar applications to comparable foreign regulatory authorities for ORLYNVAH™ or any of our product candidates.

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

Preclinical and clinical data are often susceptible to varying interpretations and analyses. Although data from 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. For example, while we ultimately received approval for ORLYNVAH™ (oral sulopenem) for the treatment of uUTIs caused by certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options, we received a CRL from the FDA on July 23, 2021 for our NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen. The CRL provided that additional data are necessary to support approval of oral sulopenem for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone and recommended that we conduct at least one additional adequate and well-controlled clinical trial, potentially using a different comparator drug. In July 2022 we reached an agreement with the FDA under the SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study was designed as a non-inferiority trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) in the Augmentin® susceptible population. In October 2023 we completed enrollment in the REASSURE clinical trial, enrolling 2,222 patients. In January 2024, we announced that ORLYNVAH™ met the primary endpoint of statistical non-inferiority to Augmentin® in the Augmentin®-susceptible population, and demonstrated statistically significant superiority versus Augmentin® in the Augmentin® susceptible population, in the REASSURE clinical trial. Additionally, though not an approvability issue, the FDA recommended in its CRL that we conduct additional non-clinical pharmacokinetic-pharmacodynamic (PK/PD) studies to support dose selection for the proposed treatment indication(s), which we completed as recommended by the FDA. We resubmitted our NDA to the FDA in April 2024 and received approval for ORLYNVAH™ for the treatment of uncomplicated uUTIs caused by certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options from the FDA in October 2024.

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

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

- we may not reach agreement on acceptable terms with all clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different trial sites;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

•the FDA, the local National Health Authorities or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

•we may have to suspend or terminate clinical trials of a product candidate for various reasons, including non-compliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;

•the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we enter into agreement for clinical and commercial supplies; or

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

If we are required to conduct additional clinical trials or other testing of any 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 any 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.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. For example, in December 2022, with the passage of the Food and Drug Omnibus Reform Act (FDORA), Congress required sponsors to develop and submit a diversity action plan (DAP) for each phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, action plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. This action raises questions about the applicability of statutory obligations to submit DAPs and the agency's current thinking on best practices for clinical development.

In addition, the regulatory landscape related to clinical trials in the European Union recently evolved. The EU Clinical Trials Regulation (CTR) which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application (CTA) to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

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. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our

product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of oral sulopenem, sulopenem or any other product candidate.

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

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. While we successfully completed the REASSURE clinical trial, we may not be able to initiate and/or continue or complete other clinical trials for 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;
- the success of 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 any clinical trials of oral sulopenem in additional indications and sulopenem may adversely affect our enrollment rates for patients in those 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 in additional indications and/or sulopenem, or slow down or halt our product development for oral sulopenem in additional indications and/or sulopenem.

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

Success in non-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot assure our shareholders that any 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 additional indications.

Although we obtained approval from the FDA for ORLYNVAH™ for the treatment of uUTIs caused by the designated microorganisms *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women who have limited or no alternative oral antibacterial treatment options on October 25, 2024, we believe that oral sulopenem and sulopenem also have the potential to treat cUTI and cIAI in humans based on the results of prior preclinical studies and clinical trials. However, we cannot guarantee that oral sulopenem and/or sulopenem will demonstrate the expected efficacy in clinical trial patients to the satisfaction of the FDA and/or other regulators in those additional indications. We also cannot guarantee that the projections made from the pharmacokinetic and pharmacodynamic models that we developed from non-clinical and clinical oral sulopenem and sulopenem studies will be validated in these clinical trials. For example, while we believe that sulopenem has the potential to treat cIAIs and cUTIs in humans based on the

results of prior preclinical studies and clinical trials, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy in our Phase 3 cIAI and cUTI clinical trials. While we believe the secondary supporting analyses and safety data in all three Phase 3 clinical trials support the potential of sulopenem in the treatment of multi-drug resistant infections, we cannot guarantee that these supporting analyses are indicative of efficacy of sulopenem in treating cIAI or cUTI.

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

Serious adverse events or undesirable side effects or other unexpected properties of ORLYNVAH™, 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 ORLYNVAH™ or any product candidate 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.

To date, sulopenem and sulopenem etzadroxil have generally been well tolerated in clinical trials conducted in healthy subjects and patients and there were no safety issues found in any patients treated with sulopenem in our prior Phase 3 clinical trials. 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.

While the active pharmaceutical ingredient in the bilayer tablet is sulopenem etzadroxil, the combination product with probenecid has not yet been tested extensively in patients. In the cIAI trial, patients received either sulopenem IV followed by sulopenem etzadroxil or ertapenem followed by ciprofloxacin/metronidazole or amoxicillin-clavulanate. Among 668 treated patients, treatment-related adverse events were observed in 6.0% and 5.1% of patients on sulopenem and ertapenem, respectively, with the most commonly reported drug-related adverse event being diarrhea, which was observed in 4.5% and 2.4% of patients on sulopenem and ertapenem, respectively. Discontinuations from treatment were uncommon for both regimens, occurring in 1.5% of patients on sulopenem and 2.1% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 7.5% of patients on sulopenem and 3.6% of patients on ertapenem. In the cUTI trial, patients received either sulopenem IV followed by sulopenem etzadroxil, if eligible for oral therapy, or ertapenem IV followed by ciprofloxacin or amoxicillin-clavulanate, if eligible for oral therapy. Among 1,392 treated patients, treatment-related adverse events were observed in 6.0% and 9.2% of patients on sulopenem and ertapenem, respectively, with the most commonly reported adverse events being headache (3.0% and 2.2%), diarrhea (2.7% and 3.0%) and nausea (1.3% and 1.6%), on sulopenem and ertapenem, respectively. Discontinuations from treatment were uncommon for both regimens, occurring in 0.4% of patients on sulopenem and 0.6% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 2.0% of patients on sulopenem and 0.9% of patients on ertapenem. In the uUTI trial known as known as Sulopenem for Resistant Enterobacteriaceae (SURE) 1, patients received either oral sulopenem or ciprofloxacin. Among 1,660 treated patients, treatment related adverse events were observed in 17.0% and 6.2% of patients on sulopenem and ciprofloxacin, respectively. The most commonly reported adverse events were diarrhea (12.4% and 2.5%), nausea (3.7% and 3.6%), and headache (2.2% and 2.2%), for sulopenem and ciprofloxacin patients, respectively. The difference in adverse events was driven by diarrhea which, in the majority of patients, was mild and self-limited. Overall discontinuations due to adverse events were uncommon on both regimens and were seen in 1.6% of patients on sulopenem and 1.0% of patients on ciprofloxacin. Serious adverse events were seen in 0.7% of patients on sulopenem with one drug-related serious adverse event due to transient angioedema and 0.2% of patients on ciprofloxacin with no drug-related serious adverse event. In the REASSURE clinical trial, patients received either ORLYNVAH™ or Augmentin®. Among 2,214 treated patients, treatment related adverse events were observed in 18.9% and 12.3% of patients on ORLYNVAH™ and Augmentin®, respectively. The most commonly reported adverse events were diarrhea (8.1% and 4.1%), nausea (4.3% and 2.9%), and headache (2.2% and 1.5%), for ORLYNVAH™ and Augmentin® patients, respectively. The difference in adverse events was driven by diarrhea which, in the majority of patients, was mild and self-limited. Overall discontinuations due to adverse events were uncommon on both regimens and were seen in 0.7% of patients on ORLYNVAH™ and 0.4% of patients on Augmentin®. Serious adverse events were seen in 0.0% of patients on ORLYNVAH™ and 0.5% of patients on Augmentin® with no drug-related serious adverse event.

While we believe these results support a positive safety and tolerability profile for sulopenem and there were no safety issues identified by the FDA in its review of ORLYNVAH™ prior to approval, in future trials there may be unforeseen serious adverse events or side effects that differ from those seen in our prior Phase 3 program. There may also be unexpected adverse events associated with probenecid that have not been seen to date. Following approval of ORLYNVAH™, we are required to report certain adverse reactions, if any, to the FDA as part of the post-marketing requirements.

If unexpected adverse events occur in any of our clinical trials, we may need to abandon development of our product candidates, or limit development to lower doses or to certain uses or subpopulations in which the undesirable side effects or other unfavorable characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing are later found to cause undesirable or unexpected side effects that prevent further development of the compound.

Undesirable side effects or other unexpected adverse events or properties of sulopenem or any of our other future product candidates could arise or become known either during clinical development or, if approved, and in the case of ORLYNVAH™, 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 sulopenem or other product candidates. If such an event occurs after such product candidates are approved, a number of potentially significant negative consequences may result, including:

•regulatory authorities may withdraw the approval of such product;

•we may be required to recall a product or change the way such product is administered to patients;

•regulatory authorities may require additional warnings on the label or impose distribution or use restrictions;

•regulatory authorities may require one or more post-marketing studies;

•regulatory authorities may require the addition of a "black box" warning;

•we may be required to implement a Risk Evaluation and Mitigation Strategy (REMS), including the creation of a medication guide outlining the risks of such side effects for distribution to patients;

•we could be sued and held liable for harm caused to patients;

•our product may become less competitive; and

•our reputation may suffer.

Additionally, if the safety warnings in our product labels are not followed, adverse medical situations in patients may arise, resulting in negative publicity and potential lawsuits, even if our products worked as we described. 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 though ORLYNVAH™ has obtained regulatory approval and we may obtain regulatory approval for other product candidates, they 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 though we have obtained FDA approval for ORLYNVAH™ and may obtain FDA or other regulatory approvals for sulopenem or any other product candidate and are able to launch ORLYNVAH™, sulopenem or any other product candidate commercially, they 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 ORLYNVAH™ and any other product candidates that obtain approval may require significant resources and may not be successful. If ORLYNVAH™, 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 ORLYNVAH™ and any product candidate for which we receive approval depends on a number of factors, including:

•the efficacy and safety of the product candidate as demonstrated in clinical trials as compared to alternative treatments;

•the potential and perceived advantages and disadvantages of the product candidates, including cost and clinical benefit relative to alternative treatments;

•relative convenience and ease of administration;

•the clinical indications for which the product candidate is approved;

•the willingness of physicians to prescribe the product;

•the willingness of hospital pharmacy directors to purchase the product for their formularies;

•acceptance by physicians, patients, operators of hospitals and treatment facilities and parties responsible for coverage and reimbursement of the product;

•the availability of coverage and adequate reimbursement by third-party payors and government authorities;

•the effectiveness of our sales and marketing efforts or those of collaborators, where we choose not to commercialize directly ourselves;

•the strength of marketing and distribution support;

•limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling or an approved REMS;

•whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;

•the approval of other new products for the same indications;

•the timing of market introduction of the approved product as well as competitive products;

•adverse publicity about the product or favorable publicity about competitive products;

•the emergence of bacterial resistance to the product; and

•the rate at which resistance to other drugs in the target infections grows.

In addition, the potential market opportunity for ORLYNVAH™ and additional sulopenem indications 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 prove to be inaccurate, then the actual market for ORLYNVAH™ and/or additional sulopenem indications could be smaller than our estimates of the potential market opportunity. If the actual market for ORLYNVAH™ and/or additional sulopenem indications is smaller than we expect, or if the product fails to achieve an adequate level of acceptance by physicians, health care payors, patients, hospitals and others in the medical community, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

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

We began operations in November 2015. Since our inception, we have devoted substantially all of our financial resources and efforts to organizing and staffing our company, business planning, raising capital, planning for potential commercialization, and research and development, including preclinical and clinical development, for our sulopenem program. While the members of our development team have successfully developed and registered other antibiotics in past roles at different companies, our company has limited experience and has not yet demonstrated an ability to successfully 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. After receiving positive data from our REASSURE clinical trial in January 2024, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing shareholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Following receipt of FDA approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized. We cannot provide any commitment regarding when or if this strategic process will result in any type of transaction however, and no assurance can be given that we will determine to pursue a potential sale, licensing arrangement or other disposition of our rights to sulopenem. In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Outside of the United States, we continue to evaluate options to maximize the value of our sulopenem program. In such circumstances, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities whether we choose to commercialize ORLYNVAH™ and/or other product candidates directly ourselves or seek to commercialize them through third-party collaboration arrangements. We may encounter unforeseen expenses, difficulties, complications and delays, and may not be successful in such a transition.

We currently have no commercial organization. If we are unable to establish and maintain sales, marketing and distribution capabilities, enter into sales, marketing and distribution agreements with third parties, or enter into a strategic transaction with a partner that has established commercial capabilities in the U.S., ORLYNVAH™ may not be successfully commercialized, if it is approved.

After receiving positive data from our REASSURE clinical trial in January 2024, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing shareholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Following receipt of FDA approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized. We cannot provide any commitment regarding when or if this strategic process will result in any type of transaction however, and no assurance can be given that we will determine to pursue a potential sale, licensing arrangement or other disposition of our rights to sulopenem. In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Outside of the United States, we continue to evaluate the options to maximize the value of our sulopenem program. If we are unable to establish and maintain sales, marketing and distribution capabilities, enter into sales, marketing and distribution agreements with third parties or enter into a strategic transaction with a partner that has established commercial capabilities in the U.S., ORLYNVAH™ may not be successfully commercialized.

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.

Other factors that may inhibit our efforts to commercialize any product directly include:

•our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;

•the inability of a health resources group to obtain access to educate physicians regarding the attributes of our future products;

•lack of adequate number of physicians to use or prescribe our 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;

•costs and expenses associated with creating an independent sales and marketing organization;

•challenges in developing a commercialization strategy or launching new drug products using a traditional marketing model following a global health crisis or pandemic;

•our inability to reach a definitive agreement for commercialization services with respect to the potential commercialization of oral sulopenem in the United States or abroad, should we choose to outsource such services to a third party;

•our inability to complete a strategic transaction with a partner that has established commercial capabilities in the U.S.; and

•our ability to raise sufficient capital to fund operations.

For those countries in which we choose not to commercialize directly ourselves, we may use collaborators that have direct sales forces and established distribution systems to assist with the commercialization of ORLYNVAH™. 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, while we are focusing on third party arrangements, we may be unsuccessful in entering into the necessary arrangements with third parties including strategic partners, or in obtaining all necessary approvals that may be required to enter into such arrangements or transactions, 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, or we are not successful in completing a strategic transaction that has established commercial capabilities in the U.S., or at all, ORLYNVAH™ and any other product candidates will not be successfully commercialized.

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

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

There are a variety of available oral therapies marketed for the treatment of multi-drug resistant infections that we expect to compete with ORLYNVAH™ and would compete with oral sulopenem in additional indications, such as levofloxacin, ciprofloxacin, nitrofurantoin, fosfomycin, amoxicillin-clavulanate, cephalexin, trimethoprim-sulfamethoxazole and pivmecillinam. ORLYNVAH™ could also compete with a few oral antibiotics currently in late-stage clinical development to treat uUTIs, including gepotidacin from GlaxoSmithKline. 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. Pricing of ORLYNVAH™, or sulopenem, if approved in additional indications, may be at a significant premium over other competitive products that are generic. This may make it difficult for ORLYNVAH™, or sulopenem, if approved in additional indications, to compete with these products.

There are several IV-administered products marketed for the treatment of infections resistant to first-line therapy for gram-negative infections, including Avycaz from AbbVie Inc and Pfizer, Vabomere from Melinta Therapeutics, Inc., Zerbaxa from Merck & Co., Zemdri from Cipla Limited, Xerava from Innovia, Inc., Recarbrio from Merck & Co, and Fetroja from Shionogi & Co., Ltd.

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

In July 2012, the Food and Drug Administration Safety and Innovation Act was passed, which included the Generating Antibiotics Incentives Now Act (the GAIN Act). The GAIN Act is intended to provide incentives for the development of new, qualified infectious disease products (QIDP). One such incentive is that, once a product receives QIDP designation and completes the necessary clinical trials and is approved by the FDA, it will be given an additional five years of exclusivity regardless of whether it is protected by a patent, provided that it is already eligible for another type of regulatory exclusivity. The FDA has designated sulopenem and oral sulopenem as QIDPs for the indications of uUTI, cUTI, cIAI, community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. In October 2024, the FDA confirmed that an additional five years of marketing exclusivity under the GAIN Act will be added to the regulatory exclusivity granted upon approval of ORLYNVAH™, resulting in a total of ten years marketing exclusivity. 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 ORLYNVAH™, oral sulopenem in additional indications or any other product candidate, the product may become subject to unfavorable pricing regulations, or third-party payor coverage and reimbursement policies that could harm our business.

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

country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

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

In the United States, sales of ORLYNVAH™, oral sulopenem in additional indications and any future 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 such 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, if approved, will be administered in a hospital setting, and that ORLYNVAH™ 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 ORLYNVAH™ and any other approved product candidates, our gross margins may decrease, which would adversely affect our ability to invest in and grow our business. Centers for Medicare and Medicaid Services (CMS) recently revised its reimbursement system for certain antibiotics in order to address challenges associated with antimicrobial resistance. Based on the final rule published on August 2, 2019, CMS is finalizing an alternative new technology add-on payment pathway (NTAP) for certain breakthrough devices, and under this policy, a QIDP product will be considered new and will not need to demonstrate that it meets the substantial clinical improvement criterion. Instead, it will only need to meet the cost criterion. CMS has also increased the NTAP percentage to 75 percent for an antimicrobial designated by the FDA as a QIDP. The potential impact of this rule on sulopenem has not yet been assessed.

On April 18, 2022, CMS released the Fiscal Year (FY) 2023 Inpatient Prospective Payment System (IPPS) proposed rule. Within each IPPS proposed rule, CMS assesses technologies that have been submitted for potential NTAP status and reconsiders the eligibility for technologies already so designated. In connection with this proposed rule, CMS assessed 13 technologies that were submitted for FY 2023 NTAP consideration through alternative application pathways. These pathways streamline the NTAP application process for (1) devices with FDA breakthrough designation, (2) drugs designated as qualified infectious disease products, and (3) technologies approved through the FDA's Limited Population Pathway for Antibacterial and Antifungal Drugs. CMS has once again proposed to approve these 13 technologies applying through the alternative pathway depending on FDA approval or clearance.

An inability to promptly obtain coverage and adequate payment rates from third-party payors for ORLYNVAH™ and any other 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 ORLYNVAH™ or sulopenem, which could affect their revenue potential.

We have developed ORLYNVAH™ for the treatment of uUTIs caused by the designated microorganisms *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women who have limited or no alternative oral antibacterial treatment options and are developing sulopenem to treat additional 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 ORLYNVAH™ 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 ORLYNVAH™ 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 ORLYNVAH™ and sulopenem if they are concerned about contributing to the rise of antibiotic resistance. If resistance to ORLYNVAH™ or sulopenem becomes prevalent, or concerns about such resistance are strong, our ability to generate revenue from ORLYNVAH™ and sulopenem could suffer.

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

Because we conduct clinical trials with human patients, we face the risk that the use of our product candidates may result in adverse side effects to patients in our clinical trials. We face even greater risks upon any commercialization of our product candidates. Although we have product liability insurance, which covers our clinical trials for up to $10.0 million, our insurance may be insufficient to reimburse us for any expenses or losses we may suffer. In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Outside of the United States, we continue to evaluate the options to maximize the value of our sulopenem program. We will need to increase our insurance coverage if we begin selling ORLYNVAH™, sulopenem or any other product candidate. We do not know whether we will be able to continue to obtain product liability coverage and obtain expanded coverage if we require it, on acceptable terms, if at all.

We may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage. Where we have provided indemnities in favor of third parties under our agreements with them, there is also a risk that these third parties could incur a liability and bring a claim under such indemnities. An individual may bring a product liability claim against us alleging that one of our product candidates or products causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

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

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

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

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

We rely on information technology systems to keep financial records, capture laboratory data, maintain clinical trial data and corporate records, communicate with staff and external parties and operate other critical functions. Our information technology systems are potentially vulnerable to disruption due to breakdown, malicious intrusion and computer viruses or other disruptive events including, but not limited to, natural disaster. If we were to experience a prolonged system disruption in our information technology systems or those of certain of our vendors, it could delay or negatively impact the development and commercialization of our sulopenem program and any future product candidates or technology, which could adversely impact our business. Although we maintain offsite back-ups of our data, if operations at our facilities were disrupted, it may cause a material disruption in our business if we are not capable of restoring function on an acceptable timeframe. In addition, our information technology systems are potentially vulnerable to data security breaches, whether by employees or others, which may expose sensitive data to unauthorized persons. Such data security breaches could lead to the loss of trade secrets or other intellectual property, or could lead to the public exposure of personal information (including sensitive personal information) of our employees and others, any of which could have a material adverse effect on our business, financial condition and results of operations.

Our technologies, systems, networks, or other proprietary information, and those of our vendors, suppliers, and other business partners, may become the target of cyberattacks or information security compromises or breaches that could result in the unauthorized release, gathering, monitoring, misuse, loss, or destruction of private, proprietary, and other information, or could otherwise lead to the disruption of our business operations. Cyberattacks are becoming more sophisticated and certain cyber incidents, such as surveillance, may remain undetected for an extended period and could lead to disruptions in critical systems or the unauthorized release of confidential or otherwise protected information. These events could lead to financial loss due to remedial actions, loss of business, disruption of operations, damage to our reputation, or potential liability, including litigation and regulatory investigations and enforcement actions. Our systems and insurance coverage for protecting against cybersecurity risks may not be sufficient. Furthermore, as cyberattacks continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate and remediate any vulnerability to cyberattacks.

Moreover, a security breach, cyberattack or privacy violation that leads to disclosure or modification of, personally identifiable information, could harm our reputation, compel us to comply with applicable European, and United States federal and/or state, breach notification laws, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to litigation and liability under laws and regulations that protect personal data, resulting in increased costs or loss of revenue. In addition, a data security breach or cyberattack 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, attacks or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer reputational damage, financial loss and other negative consequences because of lost or misappropriated information. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing ORLYNVAH™ or sulopenem in additional indications and/or any future products, if approved.

After receiving positive data from our REASSURE clinical trial in January 2024, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing shareholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Following receipt of FDA approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized. In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Outside of the United States, we continue to evaluate the options to maximize the value of our sulopenem program.

We currently do not have sales, marketing or distribution infrastructure and have limited experience as an organization in the sales, marketing, and distribution of pharmaceutical products. To achieve commercial success for ORLYNVAH™ and any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. The development of sales, marketing and distribution capabilities will require substantial resources, will be time consuming and, as this process has not been initiated for ORLYNVAH™, will delay any commercial launch. Conversely, if the commercial launch of ORLYNVAH™ or a product candidate for which we ultimately recruit a sales force and establish marketing and distribution capabilities is delayed, or does not occur for any reason, we could incur substantial costs and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these products may be substantially 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 may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

We may seek to enter into collaborations that we believe may contribute to our ability to commercialize ORLYNVAH™ or to advance development and ultimately commercialize oral sulopenem in additional indications and/or any future product candidates. We may also seek to enter into collaborations where we believe that realizing the full commercial value of our development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing ORLYNVAH™ or oral sulopenem in additional indications and/or any future product candidates that receive marketing approval.

Risks Related to Our Dependence on Third Parties

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

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

The Pfizer License gives us exclusive worldwide rights to develop, manufacture, and commercialize sulopenem etzadroxil and sulopenem, or any other prodrug of sulopenem previously identified by Pfizer as well as the right to use relevant information and regulatory documentation developed by Pfizer to support any regulatory filing worldwide. In exchange for those rights, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop, obtain regulatory approval for and commercialize sulopenem etzadroxil and sulopenem by implementing a specified development plan and providing an update on progress on an annual basis. Under the Pfizer License, we paid Pfizer a one-time non-refundable upfront fee of $5.0 million, clinical milestone payments totaling $15.0 million, upon first patient dosing of oral sulopenem and sulopenem in a Phase 3 clinical trial, and are obligated to pay Pfizer milestone payments upon the achievement of other specified regulatory and sales milestones, including a regulatory milestone payment of $20.0 million which became due upon approval of oral sulopenem for commercial sale in the United States by the FDA. We deferred this payment for a two-year period, at an annual rate of eight percent on a daily compounded basis until paid in full, as permitted pursuant to the terms of the Pfizer License. We are also obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage based on the amount of marginal net sales of each licensed product. Pfizer also received 381,922 of our Series A preferred shares (which converted to 25,461 ordinary shares in connection with our initial public offering) as additional payment for the licensed rights.

If we fail to comply with our obligations to Pfizer under the Pfizer License, Pfizer may have the right to terminate the Pfizer License, in which event we would not be able to develop, obtain regulatory approval for, manufacture or market any product or product candidate that is covered by the Pfizer License, including ORLYNVAH™ 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 commercialization of products, including ORLYNVAH™, and the development and commercialization of product candidates in certain territories. Our prospects with respect to those product candidates will depend in part on the success of those collaborations.

After receiving positive data from our REASSURE clinical trial in January 2024, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing shareholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Following receipt of FDA approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized. We cannot provide any commitment regarding when or if this strategic process will result in any type of transaction however, and no assurance can be given that we will determine to pursue a potential sale, licensing arrangement or other disposition of our rights to sulopenem. In the event our strategic process does not result in any type of

transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting.

Although we would focus our initial commercial efforts on the United States market, which we believe represents the largest market opportunity for our sulopenem program, we are also evaluating our commercialization strategy both within and outside the United States. 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 ORLYNVAH™ and any approved product, we must either build our marketing, sales, distribution, managerial and other non-technical capabilities directly, or make arrangements to outsource those functions to a commercial partner. For those countries in which we choose not to commercialize directly ourselves or through a commercial partner, we may seek to commercialize ORLYNVAH™ and/or sulopenem through collaboration arrangements. In addition, we may seek third-party collaborators for development and commercialization of other product candidates in the United States and other territories. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements could include service providers to the pharmaceutical industry, large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangements but engaged a potential commercial partner to provide pre-commercial activities and we commenced negotiations on a definitive agreement for commercialization services. Following receipt of the CRL, in order to reduce operating expenses and conserve cash resources, we halted any remaining pre-commercial activities for oral sulopenem and limited spending to essential costs required in connection with the resubmission of the NDA. There is no assurance that we will seek or be able to reach a definitive agreement for commercialization services in the future.

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 any product or product candidate that we license to a third party.

We face significant competition in seeking and obtaining appropriate collaborators. Collaborations involving our products and 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 products and 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 products and product candidates, might lead to additional responsibilities for us with respect to products and 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 products and product candidates.

Collaboration agreements may not lead to development or commercialization of products and 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 or product candidate licensed to it by us.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay a product or product candidates' potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we will need to obtain additional expertise and significant additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities directly ourselves or with a commercial partner, we may not be able to further develop our product candidates or bring any products to market including ORLYNVAH™ or continue to develop our product platform.

We may rely on third parties to perform many essential services for any products that we commercialize, including services related to warehousing and inventory control, distribution, government price reporting, customer service, accounts receivable management, cash collection, and pharmacovigilance and adverse event reporting. If these third parties fail to perform as expected or to comply with legal and regulatory requirements, our ability to commercialize our products will be significantly impacted and we may be subject to regulatory sanctions.

In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Outside of the United States, we continue to evaluate the options to maximize the value of our sulopenem program. We may retain third-party service providers to perform a variety of functions related to the sale and distribution of our products, key aspects of which will be out of our direct control. These service providers may provide key services related to warehousing and inventory control, distribution, customer service, accounts receivable management, and cash collection. If we retain a service provider, we would substantially rely on it as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical or natural damage at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired and we may be subject to regulatory enforcement action. In addition, we may engage third parties to perform various other services for us relating to pharmacovigilance and adverse event reporting, safety database management, fulfillment of requests for medical information regarding our products and related services. If the quality or accuracy of the data maintained by these service providers is insufficient, or these third parties otherwise fail to comply with regulatory requirements, we could be subject to regulatory sanctions. Additionally, we may contract with a third party to calculate and report pricing information mandated by various government programs. If a third party fails to timely report or adjust prices as required, or errors in calculating government pricing information from transactional data in our financial records, it could impact our discount and rebate liability, and potentially subject us to regulatory sanctions or False Claims Act lawsuits.

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 our product candidates or commercialize any of our products or product candidates. If they do not perform satisfactorily, our business may be materially harmed.

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

Our reliance on these third parties for clinical development activities limits our control over these activities but we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a CRO for a clinical trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the clinical trial. While we will have agreements governing their activities, we control only certain aspects of their activities and have limited influence over their actual performance. The third parties with whom we contract for execution of our GLP studies and our clinical trials play a significant role in the conduct of these studies and clinical trials and the subsequent collection and analysis of data.

Although we rely on these third parties to conduct our GLP-compliant non-clinical studies and clinical trials, we remain responsible for ensuring that each of our non-clinical studies and clinical trials are conducted in accordance with applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. The FDA and regulatory authorities in other jurisdictions also require us to comply with standards, commonly referred to as good clinical practices (GCPs), for conducting, monitoring, recording and reporting the results of clinical trials to assure that data and reported results are accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot assure our shareholders that, upon inspection, the FDA will determine that any of our clinical trials comply with GCPs. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time and resources to our 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 clinical trials and commercialization of our products and product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our products and/or 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 sulopenem for use in the conduct of our preclinical research or clinical trials or to manufacture ORLYNVAH™ for commercialization. We rely on third-party contract manufacturers to manufacture supplies of sulopenem, and we rely/expect to rely on third-party contract manufacturers to manufacture commercial quantities of ORLYNVAH™, and 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 products and/or product candidates or otherwise do not satisfactorily perform according to the terms of their agreement with us;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- the possible breach of the manufacturing agreement by the third party;
- the failure of the third-party manufacturer to comply with applicable regulatory requirements; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

We currently rely on a small number of third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our preclinical research and clinical trials. We do not have long-term agreements with any of these third parties. While we have a third-party manufacturer who can produce the ORLYNVAH™ bilayer tablet, we do not have any current contractual relationship with them for the manufacture of commercial supplies of ORLYNVAH™ or with other third-party manufacturers for 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 are in the process of negotiating agreements with third-party contract manufacturers for the commercial production of ORLYNVAH™. This process is difficult and time consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under current Good Manufacturing Practices (cGMPs), that are capable

of manufacturing our ORLYNVAH™. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay 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(s) 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 or adversely affect supplies of ORLYNVAH™ or product candidates. In addition, our manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and have a material adverse effect on our business, financial condition and results of operations.

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

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

While no issues with regard to third-party manufacturers or the manufacturing process were identified as part of the FDA review prior to approval of ORLYNVAH™, there can be no assurance that issues will not be identified in the future or that our third-party manufacturers will continue to maintain adequate quality control, quality assurance and qualified personnel and/or will continue to comply with the applicable regulatory requirements for the manufacture of our products and product candidates.

Our current and anticipated future dependence upon others for the manufacture of ORLYNVAH™ and sulopenem and any future product candidates may adversely affect our future profit margins and our ability to commercialize ORLYNVAH™ and 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 for the development of sulopenem and to commercialize ORLYNVAH™ and the know-how required to develop the IV formulation of sulopenem.

We rely heavily on the Pfizer License for intellectual property rights that are important or necessary for the development of sulopenem and to commercialize ORLYNVAH™ . 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 ORLYNVAH™ or sulopenem or other future product candidates or technologies, which could materially harm our business, financial condition, results of operations and growth prospects.

Under the Pfizer License, and we expect under certain of our future license agreements, we are responsible for prosecution and maintenance of the licensed patents and for bringing any actions against any third party for infringing on such patents. In addition, the Pfizer License requires, and we expect certain of our future license agreements would also require, us to meet certain development

thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. In addition, such license agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Disputes may arise regarding intellectual property subject to the Pfizer License or any of our future license agreements, including:

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

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

If we are unable to obtain and maintain patent protection or other intellectual property rights for ORLYNVAH™ 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 commercialize ORLYNVAH™ or develop and commercialize 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 ORLYNVAH™ or any other product candidates or technology we develop, our business, financial condition, results of operations and growth prospects could be materially harmed.

We have sought to protect our proprietary position by in-licensing patents in the United States and abroad related to oral sulopenem. We own three U.S. patents, one Japanese patent, one Korean patent and one Australian patent, with one U.S. patent, the Japanese patent, the Korean patent and the Australian patent directed to the composition of the bilayer tablet of oral sulopenem and its related preparations and/or uses, one U.S. patent directed to the method of use of oral sulopenem in treating multiple diseases, including uUTIs and one U.S. patent directed to the method of use of sulopenem etzadroxil, probenecid, and valproic acid in treating multiple diseases. We also own two pending U.S. patent applications, and 24 pending foreign patent applications, which collectively cover uses of sulopenem and probenecid and bilayer tablets of sulopenem etzadroxil and probenecid. One pending U.S. patent application and one pending Canadian patent application were recently allowed, with the allowed U.S. patent application directed to the method of use of oral sulopenem in treating uUTI, and with the allowed Canadian patent application directed to the bilayer tablet of oral sulopenem and its related preparations and/or uses.

Moreover, although we control prosecution of the patents we have licensed from Pfizer related to our sulopenem program, we may not always have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce or defend the patents, covering technology that we may license from third parties. Therefore, these patents and patent applications may not be prosecuted, maintained, enforced or defended in a manner consistent with the best interests of our business.

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

The patent position of pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of countries outside the United States may not protect our

rights to the same extent as the laws of the United States. For example, European Union (EU) patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. In addition, publications of discoveries in scientific literature often lag behind the actual discoveries, patent applications in the United States and other jurisdictions remain confidential for a period after filing, and some remain so until issued. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in the patents or pending patent applications we currently own, license or may own or license in the future, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. There is no assurance that all potentially relevant prior art relating to our patent rights has been found, and such prior art could potentially invalidate one or more of the patents we currently license or may own or license in the future or prevent a patent from issuing from one or more pending patent applications we own or may own or license in the future. There is also no assurance that prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patent rights, may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. Even if patents do successfully issue and even if such patents cover our current and future products and 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 products and product candidates that we may develop. Furthermore, even if they are unchallenged, our patents rights may not adequately protect our products, product candidates and technology, provide exclusivity for our products and 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 products or product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

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

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop and market our products and 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 products and 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 products and 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 products and product candidates or the use of our products and 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 products and product candidates. We may incorrectly determine that our products and 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 products and product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products and product candidates.

The patent protection for our products and 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 ORLYNVAH™ 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 (Hatch-Waxman Act) and our patent directed to the composition of the bilayer tablet of sulopenem etzadroxil and probenecid is due to expire no earlier than 2039, absent any extensions. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our patent rights may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

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

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of the U.S. patents we currently license and/or own may be eligible for limited patent term extension under the Hatch-Waxman Act, and similar legislation in the European Union. The Hatch-Waxman Act permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. We may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of the relevant patents or otherwise fail to satisfy applicable requirements and the length of the extension could be less than we request. To the extent we wish to pursue patent term extension based on a patent that we in-license from Pfizer or another third party, we would need the cooperation of Pfizer or the third party. Moreover, similar extensions may be available in some of the larger economic territories but may not be available in all of our markets of interest.

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

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

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

- others may be able to make compounds or formulations that are similar to oral sulopenem and sulopenem compounds or formulations but that are not covered by the claims of our patent rights;
- the patents of third parties may have an adverse effect on our business;
- we or our licensors or any future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by the issued patents that we own or have exclusively licensed;

•we or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions;

•others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;

•it is possible our pending patent applications, and any future patent applications, will not lead to issued patents or afford meaningful protection for our products and product candidates;

•issued patents that we may own in the future or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;

•our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

•third parties performing manufacturing or testing for us using our products, product candidates or technologies could use the intellectual property of others without obtaining a proper license; and

•we may not develop additional proprietary technologies that are patentable.

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

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

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the pharmaceutical industry involves both technological complexity and legal complexity. Therefore, obtaining and enforcing pharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the America Invents Act (the AIA) was signed into law on September 16, 2011, and many of its substantive changes became effective on March 16, 2013.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the U.S. Patent and Trademark Office (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 regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA. Accordingly, it is not clear what, if any, impact the AIA will have on the operation of our business and this may not be known until such time as we, or our licensors or collaboration partners, are filing patent applications for an invention or seeking to defend issued patents. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' or collaboration partners' patent applications and the enforcement or defense of our or our licensors' or collaboration partners' issued patents, all of which could have an adverse effect on our business and financial condition.

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

States or other countries may be applied retroactively to affect the ownership, validity, enforceability or term of patents we currently license or may own or license in the future.

For example, the U.S. Supreme Court's rulings on several patent cases, 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 ORLYNVAH™, 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 products and 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 ORLYNVAH™, 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 products and/or 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 and/or 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 products and/or 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 commercialize ORLYNVAH™, or further develop and commercialize one or more of our future 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 products, product candidates or intellectual property could be diminished. Accordingly, the market price of our ordinary shares may decline. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our business, ability to compete in the marketplace, financial condition, results of operations and growth prospects.

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

Filing, prosecuting and defending patents covering ORLYNVAH™, 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 ORLYNVAH™ and other product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted

narrowly and any current or future patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our ORLYNVAH™ or other 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 ORLYNVAH™ or any other product candidates in all of our expected significant foreign markets.

In Europe, a new unitary patent system took effect on June 1, 2023, which will significantly impact European patents, including those granted before the introduction of the system. Under the unitary patent system, European applications have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court (UPC). This will be a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, thereby increasing the uncertainty of any potential litigation. It is our initial belief that the UPC, while offering a cheaper streamlined process, has potential disadvantages to patent holders, such as making a single European patent vulnerable to challenges in all participating jurisdictions when challenged in a single participating jurisdiction. Given the present uncertainty, we plan to opt out of the UPC where we are able.

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

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

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

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

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

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there

are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or a patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents covering our products, our competitors might be able to enter the market, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

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

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

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

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

We have registered trademarks for “Iterum” as well as trademarks for oral sulopenem and other potential product candidates in various jurisdictions including the United States, European Union, Japan, Switzerland and Canada. If we are unable to secure registrations for our trademarks in other countries, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could adversely affect our business. Any trademark applications we have filed for our products or product candidates or may file in the future are not guaranteed to be allowed for registration, and even if they are, we may fail to maintain or enforce such registered trademarks. During trademark registration proceedings in any jurisdiction, 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 product candidates in the United States must be approved by the FDA, and in Europe by the EMA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA and the EMA each typically conduct a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA or EMA objects to any proposed proprietary product name for any future product candidates, 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 condition, results of operations and growth prospects.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

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

ORLYNVAH™, sulopenem and future product candidates 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. ORLYNVAH™ is currently our only product approved for sale in the United States.

Although we have QIDP status and fast track designation for sulopenem and oral sulopenem for the indications of uUTI, cUTI and cIAI (and for the indications of community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease) which may provide for a more rapid NDA 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. Approval policies, regulations, or the type and amount of clinical data necessary to gain approval may also change during the course of a product candidate's clinical development and may vary among jurisdictions. While we have obtained regulatory approval for ORLYNVAH™ for the treatment of uUTIs caused certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options, it is possible that we will not be able to obtain regulatory approval for sulopenem or any other product candidates or other indications that 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(s) from the FDA.

In order to obtain approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from non-clinical studies and clinical trials can be interpreted in different ways. Even if we believe that the non-clinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities.

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 CMC for the product candidate. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. The FDA has substantial discretion in the review and approval process and may refuse to accept for filing any application or may decide that our data is insufficient for approval and require additional non-clinical, clinical or other studies. Foreign regulatory authorities have differing requirements for approval of drugs with which we must comply prior to marketing. Obtaining marketing approval for marketing of a product candidate in one country does not ensure that we will be able to obtain marketing approval in other countries, but the failure to obtain marketing approval in one jurisdiction could negatively affect our ability to obtain marketing approval in other jurisdictions. The FDA or any

foreign regulatory body can delay, limit or deny approval of our product candidates or require us to conduct additional non-clinical or clinical testing or abandon a program for many reasons, including:

- the FDA or the applicable foreign regulatory agency's disagreement with the design or implementation of our clinical trials, such as the FDA stating in the CRL received in July 2021 that additional data are necessary to support approval of oral sulopenem, approval of which was ultimately obtained in October 2024;
- negative or ambiguous results from our clinical trials or results that may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory body that our product candidates are safe and effective for the proposed indication(s);
- the FDA's or the applicable foreign regulatory agency's disagreement with the interpretation of data from non-clinical studies or clinical trials;
- our inability to demonstrate the clinical and other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's or the applicable foreign regulatory agency's requirement for additional non-clinical studies or clinical trials, such as the FDA's request for additional clinical trial work in the CRL received in July 2021;
- the FDA's or the applicable foreign regulatory agency's disagreement regarding the formulation, labeling and/or the specifications for our product candidates; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

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

Moreover, principal investigators for our future clinical trials may serve as scientific advisors or consultants to us and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or a comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Further, under the Pediatric Research Equity Act (PREA), a Biologics License Application (BLA), or supplement to a BLA for certain biological products must contain data to assess the safety and effectiveness of the biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The applicable legislation in the EU also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the European Medicines Agency (EMA), or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we are seeking regulatory approval in the U.S. or the EU, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action.

While we received approval of ORLYNVAH™ for the treatment of uUTIs caused certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options without such contingencies, if we receive approval of an NDA or foreign marketing application for our future 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.

In addition, we could be adversely affected by several significant administrative law cases decided by the U.S. Supreme Court in 2024. In *Loper Bright Enterprises v. Raimondo*, for example, the court overruled *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc*., which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U.S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act (APA). Additionally, in *Corner Post, Inc. v. Board of Governors of the Federal Reserve System*, the court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, *Securities and Exchange Commission v. Jarkesy*, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and other impacts, any of which could adversely impact our business and operations.

Further, our ability to develop and market new drug products may be impacted by litigation challenging the FDA's approval of another company's drug product. In April 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS. The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone, which the FDA authorized in 2016 and 2021, were arbitrary and capricious. In June 2024, the Supreme Court reversed that decision after unanimously finding that the plaintiffs (anti-abortion doctors and organizations) did not have standing to bring this legal action against the FDA. On October 11, 2024, the Attorneys General of three states (Missouri, Idaho and Kansas) filed an amended complaint in the district court in Texas challenging FDA's actions. On January 16, 2025, the district court agreed to allow these states to file an amended complaint and continue to pursue this challenge. Depending on the outcome of this litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be delayed, undermined or subject to protracted litigation.

Finally, with the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our product candidates. The impending uncertainty could present new challenges or potential opportunities as we navigate the clinical development and approval process for our product candidates.

Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and could materially adversely impact our business and prospects.

Disruptions in the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA, EMA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. In addition, disruptions may result also events similar to the COVID-19 pandemic. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the United States facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities.

If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

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

In order to market and sell ORLYNVAH™, 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. While we received approval by the FDA for ORLYNVAH™ for the treatment of uUTIs caused certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options, 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.

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

In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. Outside of the United States, we continue to evaluate the options to maximize the value of our sulopenem program. We believe that in addition to the United States, Europe represents a significant market opportunity because of rising rates of extended spectrum ß-lactamases (ESBL) resistance.

Additionally, we could face heightened risks with respect to obtaining marketing authorization in the U.K. as a result of the withdrawal of the U.K. from the EU, commonly referred to as Brexit. The U.K. is no longer part of the European Single Market and EU Customs Union. As of January 1, 2025, the Medicines and Healthcare Products Regulatory Agency, or MHRA, is responsible for approving all medicinal products destined for the United Kingdom market (i.e., Great Britain (GB) and Northern Ireland). At the same time, a new international recognition procedure (IRP) will apply, which intends to facilitate approval of pharmaceutical products in the U.K. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators (RRs). The RRs notably include EMA and regulators in the EU/European Economic Area (EEA) member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals may force us or our collaborators to restrict or delay efforts to seek regulatory approval in the U.K. for our product candidates, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry and our business in the long term.

While we have received regulatory approval from the FDA for ORLYNVAH™ for the treatment of uUTIs caused certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options, we will be subject to ongoing obligations and continuing regulatory review, which may result in significant additional expense. Additionally, ORLYNVAH™ and any other product candidates, including 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 ORLYNVAH™ or any of our product candidates, when and if approved.

ORLYNVAH™ and any other product candidate, including 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. For example, in addition to reporting of adverse reactions to ORLYNVAH™, post marketing requirements for ORLYNVAH™ also include conducting a U.S. surveillance study over a five-year period after the introduction of ORLYNVAH™ to the market to determine if resistance has increased or decreased susceptibility to ORLYNVAH™ is occurring in the target population of bacteria identified in the approved label for ORLYNVAH™.

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.

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

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

Finally, our ability to develop and market new drug products including ORLYNVAH™ may be impacted by ongoing litigation challenging the FDA's approval of mifepristone. Specifically, on April 7, 2023, the U.S. District Court for the Northern District of Texas stayed the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various conditions adopted under a REMS. In reaching that decision, the district court made a number of findings that may negatively impact the development, approval and distribution of drug products in the U.S. Among other determinations, the district court held that plaintiffs were likely to prevail in their claim that FDA had acted arbitrarily and capriciously in approving mifepristone without sufficiently considering evidence bearing on whether the drug was safe to use under the conditions identified in its labeling. Further, the district court read the standing requirements governing litigation in federal court as permitting a plaintiff to bring a lawsuit against the FDA in connection with its decision to approve an NDA or establish requirements under a REMS based on a showing that the plaintiff or its members would be harmed to the extent that FDA's drug approval decision effectively compelled the plaintiffs to provide care for patients suffering adverse events caused by a given drug.

On April 12, 2023, the district court decision was stayed, in part, by the U.S. Court of Appeals for the Fifth Circuit. Thereafter, on April 21, 2023, the U.S. Supreme Court entered a stay of the district court's decision, in its entirety, pending disposition of the appeal of the district court decision in the Court of Appeals for the Fifth Circuit and the disposition of any petition for a writ of certiorari to or the Supreme Court. The Court of Appeals for the Fifth Circuit held oral argument in the case on May 17, 2023 and, on

August 16, 2023, issued its decision. The court declined to order the removal of mifepristone from the market, finding that a challenge to the FDA's initial approval in 2000 is barred by the statute of limitations. But the Appeals Court did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone that FDA authorized in 2016 and 2021 were arbitrary and capricious. On September 8, 2023, the Justice Department and a manufacturer of mifepristone filed petitions for a writ of certiorari, requesting that asked the U.S. Supreme Court to review the Appeals Court decision. On December 13, 2023, the Supreme Court granted these petitions for writ of certiorari for the appeals court decision.

Similar restrictions apply to the approval of our products in the European Union. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the European Union and are also subject to EU Member State laws.

Accordingly, in connection with our currently approved product and assuming we, or our collaborators, receive marketing approval for one or more other product candidates, we, and our collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we, and our collaborators, are not able to comply with post-approval regulatory requirements, our or our collaborators' ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any regulatory approval to market our products will be limited by indication. If we fail to comply or are found to be in violation of FDA regulations restricting the promotion of our products for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA, EMA, MHRA and other government agencies. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. Physicians may nevertheless prescribe our products off-label to their patients in a manner that is inconsistent with the approved label. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of our products for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. For example, in January 2025, the FDA published final guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use. In addition, under some relatively recent guidance from the FDA and the Pre-Approval Information Exchange Act (PIE Act) signed into law as part of the Consolidated Appropriations Act of 2023, companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We may engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. We will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products.

In recent years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission (FTC), and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDCA, the False Claims Act, the Prescription Drug Marketing Act and anti-kickback laws and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "qui tam" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim or caused a false claim to be submitted to the government for payment. The person bringing a qui tam suit is entitled to a share of any recovery or settlement. Qui tam suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

Any relationships we may have with customers, healthcare providers and professionals and third-party payors, among others, will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties, including criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we are able to obtain marketing approval. Any arrangements we have with healthcare providers, third-party payors and customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws and regulations may constrain the business or financial arrangements and relationships through which we conduct clinical research, market, sell and distribute any products for which we obtain marketing approval. These include the following:

- *Anti-Kickback Statute*. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward or in return for, either the referral of an individual for or the purchase, lease or order of a good, facility, item or service for which payment may be made under a federal healthcare program such as Medicare and Medicaid.

- *False Claims Laws.* The federal false claims and civil monetary penalties laws, including the federal civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions against individuals or entities for, among other things, knowingly presenting or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties.

- *Health Insurance Portability and Accountability Act of 1996 (HIPAA).* HIPAA imposes criminal and civil liability for, among other things, executing a scheme or making materially false statements in connection with the delivery of or payment for health care benefits, items or services. Additionally, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations on covered entities and their business associates that perform certain functions or activities that involve the use or disclosure of protected health information on their behalf, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information.

- *Transparency Requirements.* The federal Physician Payments Sunshine Act requires 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 specific exceptions, to report annually to CMS information related to payments or transfers of value made to physicians, other healthcare providers and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members.

- *Analogous State and Foreign Laws.* Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors and are generally broad and are enforced by many different federal and state agencies as well as through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that any business arrangements we have with third parties and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or

similar agreement to resolve allegations of non-compliance with these laws, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States. In addition, payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

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 state levels that seek to reduce healthcare costs. For example, in March 2010 the Patient Protection and Affordable Care Act (as amended by the Health Care and Education Reconciliation Act) (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.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013.

The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Under current legislation, the actual reductions in Medicare payments may vary up to 4%. The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 (PAYGO), sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriation Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017 (TCJA), Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the PPACA brought by several states without specifically ruling on the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

In the EU, on December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment (HTA), amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and

continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when approved.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In addition, in October 2020, the Department of Health and Human Services (HHS) and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program (SIP), to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America (PhRMA) but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Seven states (Colorado, Florida, Maine, New Hampshire, New Mexico, Texas and Vermont) have passed laws allowing for the importation of drugs from Canada. North Dakota and Virginia have passed legislation establishing workgroups to examine the impact of a state importation program. As of October 2024, five states (Colorado, Florida, Maine, New Hampshire and New Mexico) had submitted Section 804 Importation Program proposals to the FDA. Vermont has submitted a concept letter to the HHS. On January 5, 2024, the FDA approved Florida's plan for Canadian drug importation. That state now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which must be approved by the FDA. The state will also need to relabel the drugs and perform quality testing of the products to meet FDA standards.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022 (IRA) was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least nine years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, the HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. On October 2, 2024, in final guidance, CMS indicated that it would announce the selection of up to 15 additional drugs covered by Part D for the second cycle of negotiations by February 1, 2025. That announcement was made on January 17, 2025. This second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027.

Further, the new legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce (Chamber), Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. There have been various decisions by the courts considering these cases since they were filed. The HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

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

Finally, in the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved.

In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the European Union or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain

regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Reporting and payment obligations under the Medicaid Drug Rebate Program and other governmental drug pricing programs are complex and may involve subjective decisions. Any failure to comply with those obligations could subject us to penalties and sanctions.

As a condition of reimbursement by various federal and state health insurance programs, pharmaceutical companies are required to calculate and report certain pricing information to federal and state agencies. The regulations governing the calculations, price reporting and payment obligations are complex and subject to interpretation by various government and regulatory agencies, as well as the courts. Reasonable assumptions have been made where there is lack of regulations or clear guidance and such assumptions involve subjective decisions and estimates. Pharmaceutical companies are required to report any revisions to our calculation, price reporting and payment obligations previously reported or paid. Such revisions could affect liability to federal and state payers and also adversely impact reported financial results of operations in the period of such restatement.

Uncertainty exists as new laws, regulations, judicial decisions, or new interpretations of existing laws, or regulations related to our calculations, price reporting or payments obligations increases the chances of a legal challenge, restatement or investigation. If a company becomes subject to investigations, restatements, or other inquiries concerning compliance with price reporting laws and regulations, it could be required to pay or be subject to additional reimbursements, penalties, sanctions or fines, which could have a material adverse effect on the business, financial condition and results of operations. In addition, it is possible that future healthcare reform measures could be adopted, which could result in increased pressure on pricing and reimbursement of products and thus have an adverse impact on financial position or business operations.

Further, state Medicaid programs may be slow to invoice pharmaceutical companies for calculated rebates resulting in a lag between the time a sale is recorded and the time the rebate is paid. This results in a company having to carry a liability on its consolidated balance sheets for the estimate of rebate claims expected for Medicaid patients. If actual claims are higher than current estimates, the company's financial position and results of operations could be adversely affected.

In addition to retroactive rebates and the potential for 340B Program refunds, if a pharmaceutical firm is found to have knowingly submitted any false price information related to the Medicaid Drug Rebate Program to CMS, it may be liable for civil monetary penalties. Such failure could also be grounds for CMS to terminate the Medicaid drug rebate agreement, pursuant to which companies participate in the Medicaid program. In the event that CMS terminates a rebate agreement, federal payments may not be available under government programs, including Medicaid or Medicare Part B, for covered outpatient drugs.

Additionally, if a pharmaceutical company overcharges the government in connection with the Family Self-Sufficiency Program or Tricare Retail Pharmacy Program, whether due to a misstated Federal Ceiling Price or otherwise, it is required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against a company under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

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

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

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

recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union member states, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain European Union member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union member states. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

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

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

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation (GDPR), which took effect across all member states of the EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data (including health and other sensitive data), including the following: to provide information to individuals regarding data processing activities; to implement safeguards to protect the security and confidentiality of personal data; to make a mandatory breach notification in certain circumstances; and to take certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater. The GDPR also confers a private right of action on data subjects to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data adding to the complexity of processing personal data in the European Union.

In July 2020, the Court of Justice of the European Union (CJEU) invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. Additionally, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-US Privacy Shield. The European Union initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business at the international level.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act—which went into effect on January 1, 2020—is

creating similar risks and obligations as those created by GDPR, though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

In addition to California, at least eighteen other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect over the next few years. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2024 legislative sessions that will go into effect in 2025 and beyond, including New Hampshire and New Jersey. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, Washington state passed a health privacy law in 2023 that regulates the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation in 2025. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act. The rise in these types of lawsuits creates potential risk for our business.

If we fail to comply with applicable privacy laws, including applicable the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In recent months, the Officer of Civil Rights (OCR) has been especially active in enforcing the HIPAA rules. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems. Additionally, OCR is looking to amend the HIPAA Security Rule, which (if and when finalized) could create additional compliance obligations and risk for our business.

In addition to potential enforcement by the HHS, we could also be potentially subject to privacy enforcement from the FTC. The FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the FTC Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security. We will need to account for the FTC's evolving rules and guidance for proper privacy and data security practices in order to mitigate risk for a potential enforcement action, which may be costly. Finally, both the FTC and HHS's enforcement priorities (as well as those of other federal regulators) may be impacted by the change in administration and new leadership. These shifts in enforcement priorities may also impact our business.

There are also increased restrictions at the federal level relating to transferring sensitive data outside of the U.S. to certain foreign countries. For example, in 2024, Congress passed H.B. 815, which included the Protecting Americans' Data from Foreign Adversaries Act of 2024. This law creates certain restrictions for entities that disclose sensitive data (including potential health data) to countries such as China. Failure to comply with these rules can lead to a potential FTC enforcement action. Additionally, the Department of Justice recently finalized a rule implementing Executive Order 14117, which creates similar restrictions related to the transfer of sensitive US data to countries such as China. These data transfer restrictions (and others that may pass in the future) may create operational challenges and legal risks for our business.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities, and

could lead to government enforcement actions, private litigation and significant fines and penalties against us, all of which could increase our cost of doing business and have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws regarding privacy and security of personal information could expose us to fines and penalties under such laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Further, we cannot assure you that our third-party service providers with access to our or our customers', suppliers', trial patients' and employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations and financial condition. We cannot assure you that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, storage and transmission of such information.

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

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

Risks Related to Employee Matters and Managing Growth

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

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Corey N. Fishman, our Chief Executive Officer, as well as the other principal members of our management 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 have in the past, and may continue to do so in the future, relied 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 may encounter difficulties in managing growth, which could disrupt our operations.

We could experience growth in the number of our employees and the scope of our operations particularly in the areas of manufacturing, regulatory affairs, sales, marketing and health resources. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to 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 any 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. Any growth experienced 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 such 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.

In addition, we have and may continue to need to adjust the size of our workforce as a result of changes to our expectations for our business, which can result in diversion of management attention, disruptions to our business, and related expenses.

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, public health crises, or pandemics; and
- failure to comply with Office of Foreign Asset Control rules and regulations and the FCPA.

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

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

In the future, we may enter into transactions to acquire other businesses, products or technologies. Any such proposed acquisitions may be subject to the consent of certain holders of the RLNs in accordance with the terms and conditions of the RLN Indenture. If we do identify suitable candidates for acquisition, we may not be able to make such acquisitions on favorable terms, or at all, and we may not be able to obtain approval of or consent to such acquisitions from holders of the RLNs. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our ordinary shares or other equity securities to the shareholders of the acquired company, which would reduce the percentage ownership of our then current shareholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive 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

As used in this section, Risks Related to Taxation, the term "U.S. Holder" means a beneficial owner of our ordinary shares that is, for U.S. federal income tax purposes, (1) an individual who is a citizen or resident of the United States, (2) a corporation (or entity treated as a corporation) created or organized in or under the laws of the United States, any state thereof, or the District of Columbia or otherwise treated as a "domestic corporation" for such purposes, (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. If a partnership or other pass-through entity holds our ordinary shares, the U.S. federal income tax treatment of a partner in that partnership or entity generally will depend upon the status of that partner and the activities of that partnership or entity.

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

We were a passive foreign investment company (PFIC) for U.S. federal income tax purposes for our taxable year ended December 31, 2017. Based on our gross income and average value of our gross assets, we do not believe we (or our wholly owned non-U.S. subsidiaries) were a PFIC for the taxable year ended December 31, 2018 or for any subsequent completed taxable year. We do not expect to be a PFIC for the taxable year ending December 31, 2024; however, our status, and the status of our non-U.S. subsidiaries, in any taxable year will depend on our assets and activities as determined at various times throughout that taxable year. As our PFIC status is a factual determination made annually after the end of each taxable year, there can be no assurances as to that status for the current taxable year or any future taxable year.

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

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

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

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

In certain circumstances a U.S. Holder may make a qualified electing fund (QEF election), under the U.S. federal income tax laws with respect to that holder's interest in a PFIC. Such an election may mitigate some of the adverse U.S. federal income tax consequences that could otherwise apply to a U.S. Holder under the excess distribution regime. However, we do not expect to provide

U.S. Holders with the information necessary to make a valid QEF election, and U.S. Holders should therefore assume that a QEF election will not be available.

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Ordinary Shares

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

Our ordinary shares began trading on the Nasdaq Global Market on May 25, 2018 and on December 23, 2020, we transferred the listing of our ordinary shares to The Nasdaq Capital Market.Given the relatively limited trading history of our ordinary shares and the intermittent volume of trading of our ordinary shares during that time, there is a risk that an active trading market for our shares may not be sustained, which could put downward pressure on the market price of our ordinary shares and thereby affect the ability of shareholders to sell their shares. An inactive trading market for our ordinary shares may also impair our ability to raise capital to continue to fund our operations by issuing shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

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

Our share price has been and may continue to be volatile. The daily closing market price for our ordinary shares has varied between a high price of $2.91 on December 9, 2024, and a low price of $0.9099 on October 9, 2024, in the twelve-month period ending on February 5, 2025. During this time, the price per ordinary share has ranged from an intra-day low of $0.808 per share to an intra-day high of $3.02 per share. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their ordinary shares at or above the price paid for the shares.

We may continue to incur rapid and substantial increases or decreases in our stock price in the foreseeable future that may not coincide in timing with the disclosure of news or developments by or affecting us. Accordingly, the market price of our ordinary shares may fluctuate dramatically, and may decline rapidly, regardless of any developments in our business.

The trading price of our ordinary shares could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The market price for our ordinary shares may be influenced by those factors discussed elsewhere in this "Risk Factors" section of this document and others, such as:

- results from, and any delays in, clinical trials;
- announcements of regulatory approval, failure to obtain regulatory approvals or receipt of a "complete response letter" from the FDA with respect to any of our product candidates;
- announcements with respect to the outcome, impact, effects or results of our evaluation of corporate, strategic, financial and financing alternatives, including the terms, timing, structure, value, benefits and costs of any corporate, strategic, financial or financing alternative and our ability to complete one at all;
- our need to raise additional funds;
- announcements relating to changes to our capital structure including a reorganization, recapitalization, share split or reverse share split, exchange of shares, or any similar equity restructuring transaction;
- the sentiment of retail investors including the perception of our clinical trial results by such retail investors, which investors may be subject to the influence of information provided by social media, third party investor websites and independent authors distributing information on the internet;
- delays in the commercialization of ORLYNVAH™, sulopenem or any future product candidates;
- manufacturing and supply issues related to our development programs and commercialization of ORLYNVAH™, 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, or withdrawal of coverage, 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, management, or key scientific personnel;
- 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 ORLYNVAH™, sulopenem or future products;
- failure to comply with the Nasdaq Capital Market continued listing requirements;
- market conditions in the healthcare market in general, or in the antibiotics segment in particular, including performance of our competitors;
- publication of research reports about us or our industry, or antibiotics in particular;
- changes in the market valuations of similar companies;

•sales of large blocks of our ordinary shares by our existing shareholders; and

•general economic conditions in the United States and abroad, including resulting from geo-political actions, including war and terrorism, natural disasters, including earthquakes, hurricanes, typhoons, floods and fires, public health crises, or pandemics.

In addition, the stock market in general, or the market for equity securities in our industry, may experience extreme volatility unrelated to our operating performance. In recent years, the market for pharmaceutical and biotechnology companies in particular has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose shares are experiencing those price and volume fluctuations. These broad market fluctuations may adversely affect the trading price or liquidity of our ordinary shares regardless of our actual operating performance. 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.

The volatility of our shares and shareholder base may hinder or prevent us from engaging in beneficial corporate initiatives.

Our shareholder base is comprised of a large number of retail (or non-institutional) investors, which creates more volatility since shares change hands frequently. In accordance with our governing documents and applicable laws, there are a number of initiatives that require the approval of shareholders at an annual or extraordinary general meeting of shareholders. To hold a valid meeting, a quorum comprised of one or more Members (as defined in our Amended and Restated Constitution) whose name is entered in our register of members as a registered holder of our ordinary shares, present in person or by proxy (whether or not such Member actually exercises his voting rights in whole, in part or at all), holding not less than a majority of our issued and outstanding ordinary shares entitled to vote at a meeting of shareholders, is required. A record date is established to determine which shareholders are eligible to vote at the meeting, which record date must not be more than 60 days prior to the date of the meeting. Since our shares change hands frequently, there can be a significant turnover of shareholders between the record date and the meeting date which makes it harder to get shareholders to vote. While we make every effort to engage retail investors, such efforts can be expensive and the frequent turnover creates logistical issues for obtaining shareholder approval. Further, retail investors tend to be less likely to vote in comparison to institutional investors. Failure to secure sufficient votes may impede our ability to move forward with initiatives that are intended to grow the business and create shareholder value or prevent us from engaging in such initiatives at all. If we find it necessary to delay or adjourn meetings or to hold multiple meetings to secure sufficient shareholder votes, it will be time consuming and we will incur additional costs.

If we fail to comply with the listing requirements of the Nasdaq Capital Market, we may be delisted and the price of our ordinary shares, our ability to access the capital markets and our financial condition could be negatively impacted and the delisting of our ordinary shares would result in an event of default and/or fundamental change under our debt instruments.

Our ordinary shares are currently listed for quotation on the Nasdaq Capital Market. To maintain the listing of our ordinary shares on the Nasdaq Capital Market, we are required to meet certain listing requirements, including, among others:

•a minimum closing bid price of $1.00 per share, and

•a market value of publicly held shares (excluding shares held by our officers, directors and 10% or more shareholders) of at least $1.0 million.

In addition to the above requirements, we must meet at least one of the following requirements:

•shareholders' equity of at least $2.5 million; or

•a market value of listed securities of at least $35 million; or

•net income from continuing operations of $500,000.

Although we have been able to regain compliance with Nasdaq listing requirements within the manner and time periods prescribed by Nasdaq in the past, there can be no assurance that we will be able to maintain compliance with the Nasdaq Capital Market continued listing requirements in the future or regain compliance with respect to any future deficiencies. This could impair the liquidity and market price of our ordinary shares. In addition, the delisting of our ordinary shares from a national exchange could have a material adverse effect on our access to capital markets, and any limitation on market liquidity or reduction in the price of our ordinary shares as a result of that delisting could adversely affect our ability to raise capital on terms acceptable to us, or at all.

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

As part of a private placement which closed in January 2020 (the Private Placement) and subsequent 2020 Rights Offering, Iterum Bermuda issued RLNs which entitle the holders thereof to certain payments in connection with commercial sales of sulopenem. Holders of RLNs are entitled to payments based solely on a percentage of our net revenues from U.S. sales of specified sulopenem products (Specified Net Revenues). Payments will be due within 75 days of the end of each six-month payment measuring period (each, a Payment Measuring Period), beginning with the Payment Measuring Period ending June 30, 2020 until (i) the "Maximum Return" (as defined below) has been paid in respect of the RLNs, or (ii) December 31, 2045 (the End Date), or (iii) December 31, 2025, in the event that we have not yet received FDA approval with respect to one or more specified sulopenem products by such date. The aggregate amount of payments in respect of all RLNs during each Payment Measuring Period will be equal to the product of total Specified Net Revenues earned during such period and the applicable payment rate, being 15%.

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

Iterum Bermuda may at any time redeem for cash all, but not less than all, of the RLNs, at its option. The redemption price per RLN will be equal to the Maximum Return for each RLN, less payments made through and including the redemption date, plus certain accrued but unpaid default interest (if any). Upon a change of control of our company, we will require the ultimate beneficial owner or owners controlling the acquiring person or persons to guarantee the obligations of Iterum Bermuda under the RLN Indenture.

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

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

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

The issuance of additional ordinary shares may dilute our existing shareholders' level of ownership in our Company or require us to relinquish rights.

Any issuance of securities we may undertake, whether in the future to raise additional capital or upon exchange or exercise of outstanding convertible securities, 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.

The outstanding warrants that we issued the purchasers and/or the designees of the placement agent and underwriter, as applicable, in connection with the June 3, 2020 Offering, the June 30, 2020 Offering, the October 2020 Offering, the February 2021 Underwritten Offering, the February 2021 Registered Direct Offering and the 2024 Rights Offering, are exercisable at any time until a specified expiration date, and any exercise of outstanding warrants will increase the number of shares outstanding, which may dilute the ownership percentage or voting power of our shareholders.

Similarly, the outstanding warrants that we issued SVB and Life Sciences Fund II LLC in connection with the secured credit facility we had in place with SVB are exercisable at any time until April 27, 2028, and any exercise of such warrants will increase the number of shares outstanding, which may dilute the ownership percentage or voting power of our shareholders. Additionally, the exercise of outstanding options and vesting of restricted share units under our equity incentive plans or equity inducement incentive

plan or exercise of other outstanding warrants for ordinary shares may also dilute the ownership percentage or voting power of our shareholders.

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

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

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

A portion of our outstanding ordinary shares is currently restricted as a result of federal securities laws but can be sold at any time subject to applicable volume limitations.

In addition, on October 7, 2022, we entered into the Sales Agreement with HC Wainwright, as agent, pursuant to which we may offer and sell ordinary shares for aggregate gross sales proceeds of up to $16.0 million (subject to the availability of ordinary shares), from time to time through HC Wainwright by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act. On December 10, 2024 we filed a prospectus supplement with the SEC pursuant to which we may offer and sell ordinary shares having an aggregate offering price of up to an additional $25.0 million through HC Wainwright pursuant to the Sales Agreement. We cannot predict if and when shares sold pursuant to the Sales Agreement, if any, will be resold in the public markets. Any of our outstanding shares that are not restricted as a result of securities laws may be resold in the public market without restriction unless purchased by our affiliates.

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

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

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

•that it did not have jurisdiction;

•that it was not the appropriate forum for such proceedings;

•that, applying Irish conflict of law rules, U.S. law (including U.S. securities laws) did not apply to the relationship between the shareholder and us or our directors and officers; or

•that the U.S. securities laws were of a penal nature and violated Irish public policy and should not be enforced by the Irish court.

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

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

•U.S. courts must have had jurisdiction in relation to the particular defendant according to Irish conflict of law rules (the submission to jurisdiction by the defendant would satisfy this rule); and

•the judgment must be final and conclusive and the decree must be final and unalterable in the court which pronounces it.

A judgment can be final and conclusive even if it is subject to appeal or even if an appeal is pending. But where the effect of lodging an appeal under the applicable law is to stay execution of the judgment, it is possible that in the meantime the judgment may

not be actionable in Ireland. It remains to be determined whether final judgment given in default of appearance is final and conclusive. Irish courts may also refuse to enforce a judgment of the U.S. courts which meets the above requirements for one of the following reasons:

- the judgment is not for a definite sum of money;
- the judgment was obtained by fraud;
- the enforcement of the judgment in Ireland would be contrary to natural or constitutional justice;
- the judgment is contrary to Irish public policy or involves certain U.S. laws which will not be enforced in Ireland; or
- jurisdiction cannot be obtained by the Irish courts over the judgment debtors in the enforcement proceedings by personal service in Ireland or outside Ireland under Order 11 of the Irish Superior Courts Rules.

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

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

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

As a publicly traded company, we have incurred and will continue to incur significant additional legal, accounting and other expenses compared to historical levels. In addition, new and changing laws, regulations and standards relating to corporate governance and public disclosure, including the Dodd-Frank Wall Street Reform and Consumer Protection Act and the rules and regulations promulgated and to be promulgated thereunder, as well as under the Sarbanes-Oxley Act of 2002 (the Sarbanes-Oxley Act), the Jumpstart Our Business Startups Act of 2012 (the JOBS Act) and the rules and regulations of the SEC and the Nasdaq Capital 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 continue 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 "smaller reporting company," and the reduced disclosure requirements applicable to smaller reporting companies may make our ordinary shares less attractive to investors.

We are a "smaller reporting company" as defined in Rule 12b-2 promulgated under the Securities Exchange Act of 1934, as amended (the Exchange Act). We may remain a smaller reporting company until we have a non-affiliate public float of at least $250 million and annual revenues of at least $100 million or a non-affiliate public float of at least $700 million, each as determined on an annual basis. For so long as we remain a smaller reporting company, we are permitted to take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. These provisions include:

- an exemption from compliance with the auditor attestation requirement of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, on the design and effectiveness of our internal controls over financial reporting; and
- reduced disclosure about our executive compensation arrangements.

Investors may find our ordinary shares less attractive if we rely on certain or all of these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may decline or become more volatile.

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

As a public company, we are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of the applicable listing standards of the Nasdaq Capital Market. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Our current controls and any new controls that we develop may become inadequate because of changes in conditions in our business. Further, weaknesses in our disclosure controls and internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective controls or any difficulties encountered in their implementation or improvement could harm our results of operations or cause us to fail to meet our reporting obligations and may result in a restatement of our consolidated financial statements

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

Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain a smaller reporting company with less than $100 million in revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we engaged and continue to engage in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. Additionally, we will be unable to issue securities in the public markets through the use of a shelf registration if we are not in compliance with Section 404.

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

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

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

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

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

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

- dividing our board of directors into three classes, with each class serving a staggered three-year term;
- permitting our board of directors to adopt a shareholder rights plan upon such terms and conditions as it deems expedient and in our best interests;
- permitting our board of directors to issue preference shares, with such rights, preferences and privileges as they may designate;
- establishing an advance notice procedure for shareholder proposals to be brought before an annual meeting, including proposed nominations of persons for election to our board of directors; and

•imposing particular approval and other requirements in relation to certain business combinations.

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

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

The RLN Indenture prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the RLNs, the RLN Indenture and the guarantees and the RLN Indenture prohibits us from selling, transferring or assigning certain assets and prohibits Iterum Bermuda, the Guarantors or any of our significant subsidiaries from undergoing a change of control, other than in connection with a change of control of us. These and other provisions in the RLN Indenture could deter or prevent a third party from acquiring us even when the acquisition may be favorable to the holders of our ordinary shares.

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

Following the authorization for trading of our ordinary shares on the Nasdaq Global Market on May 25, 2018, we became subject to the Irish Takeover Panel Act, 1997, Irish Takeover Rules 2022 (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) the redemption or repurchase of securities by the Company (save in certain circumstances), (iii) material acquisitions or disposals, (iv) entering into contracts other than in the ordinary course of business, or (v) 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, then the acquirer and/or, in certain circumstances, its concert parties would be required (except with the consent of the Irish Takeover Panel) to make an offer for all of 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 (known as a mandatory cash offer). 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 was to increase that person's percentage of the voting rights by 0.05% within any 12 month period.

Under the Irish Takeover Rules, certain separate concert parties are presumed to be acting in concert. Our board of directors and their relevant family members, related trusts and "controlled companies" are presumed to be acting in concert with any corporate shareholder who holds 20% or more of our shares. The application of these presumptions may result in restrictions upon the ability of any such concert parties and/or members of our board of directors to acquire more of our securities, including under any executive incentive arrangements. We, or any such holders, may consult with the Irish Takeover Panel from time to time 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 would overrule this presumption. Accordingly, the application of the Irish Takeover Rules may restrict the ability of certain of our shareholders and directors to acquire our ordinary shares.

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 a resolution approved by not less than 50% of the votes cast at a general meeting of our shareholders. Additionally, subject to specified exceptions, Irish law grants statutory pre-emption rights to existing shareholders where shares are being issued for cash consideration but allows shareholders to disapply such statutory pre-emption rights either in our Articles of Association or by way of a resolution approved by not less than 75% of the votes cast at a general meeting of our shareholders. Such disapplication can either be generally applicable or be in respect of a particular allotment of shares. Accordingly, at an extraordinary meeting of our shareholders on October 8, 2024, our shareholders authorized the board to issue new shares, and to disapply statutory pre-emption rights for such issuances up to the amount of our authorized but unissued share capital until May 3, 2028. The authorization of the directors to issue shares and the disapplication of statutory

pre-emption 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, or be approved without limitations, which could limit our ability to issue equity and thereby adversely affect the holders of our securities.

We could be subject to securities class action litigation that could divert management's attention and harm our business.

In the past, securities class action litigation has often been brought against a company following a significant business transaction, such as the announcement of a financing or a strategic transaction, or the announcement of a negative event, such as a negative regulatory decision. These events may also result in investigations by the SEC. We may be exposed to such litigation or investigation even if no wrongdoing occurred. Litigation and investigations are usually expensive and divert management's attention and resources, which could adversely affect our cash resources and/or our ability to consummate a potential strategic transaction.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item IC. Cybersecurity.

Risk Management and Strategy

Identifying, assessing, and managing material cybersecurity risks is an important component of our overall risk management program. Our cybersecurity strategy is designed to prioritize detecting and responding to threats and effective management of security risks.

To implement our cybersecurity strategy, we maintain various safeguards and undertake certain cybersecurity programs to secure the data we hold, including encrypting sensitive data, utilizing a robust 24/7/365 security monitoring system, monitoring our information systems for potential vulnerabilities, conducting data security assessments of third-party service providers as part of vendor management, and providing employee testing and training, including phishing tests, general cybersecurity awareness training and business team-focused tabletop exercises.

We have also adopted an Incident Response Procedure (the IR Plan) that outlines the legal and governance processes for identifying, assessing and managing material risks to privacy and security. An incident response team and various senior members of management are responsible for carrying out the IR Plan, in conjunction with our third-party IT service provider.

We do not believe that there are currently any risks from cybersecurity threats that are reasonably likely to materially affect the Company or its business strategy, results of operations or financial condition. Risks from cybersecurity threats may, in the future, among other things, cause material disruptions to our operations, which may materially affect our results of operations and/or financial condition. For more information about these risks, see the risk factor titled "If we experience a significant disruption in our information technology systems, or breaches of data security, or become the target of a cyberattack, our business could be adversely affected" under Item 1A of this Annual Report on Form 10-K.

Governance related to Cybersecurity Risks

Our board of directors, as a whole and through its committees, has responsibility for the oversight of risk management. Our board of directors has assigned oversight of cybersecurity risk management to the Audit Committee.

Management, including the Chief Executive Officer (CEO), Chief Financial Officer (CFO) and Senior Vice President, Legal Affairs, are responsible for the day-to-day management of risks we face and are involved in implementing the IR Plan, with assistance from our third-party IT service provider (the IT Provider). Pursuant to the terms of our IR Plan, in the event of a material or potentially material cybersecurity event, senior members of management must be promptly informed of such event and oversee triage, response, and disclosure efforts. If a potential cybersecurity incident is identified, the IT Provider must promptly inform the Incident Response Team (IRT), comprised of a designated key individual from the IT Provider, our Senior Vice President, Legal Affairs and our Senior Vice President and Head of Clinical Development. The IRT must then conduct an initial triage of the event in accordance with the IR Plan and, as needed, escalate such event to the CEO and CFO to determine the appropriate course of action including determining whether the event is deemed material for the purpose of requiring disclosure on a Current Report on Form 8-K filing with the SEC.

Our Audit Committee receives periodic updates and provides feedback on from our management regarding cybersecurity matters, including any cybersecurity risks and/or any incidents and related responses, and is notified between such updates regarding significant new cybersecurity threats or incidents. The board of directors receives regular reports from the Audit Committee addressing cybersecurity as part of our overall risk management program.

Item 2. Properties.

We lease office space in Old Saybrook, Connecticut. Our lease extends through June 2025.

We also lease office space in Chicago, Illinois. Our lease extends through May 31, 2025.

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

Item 3. Legal Proceedings.

We are not currently subject to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Between May 25, 2018 and December 22, 2020, our ordinary shares were publicly traded on The Nasdaq Global Market under the symbol "ITRM". On December 23, 2020, we transferred the listing of our ordinary shares to The Nasdaq Capital Market. Prior to May 25, 2018, there was no public market for our shares.

Holders of Record

On January 31, 2025, we had 12 shareholders of record of our ordinary shares. The actual number of shareholders is greater than this number of record holders and includes shareholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

Dividends

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

Recent Sales of Unregistered Securities

During the period January 1, 2024 through December 31, 2024, we did not issue any equity securities that were not registered under the Securities Act of 1933, as amended, other than pursuant to transactions previously disclosed in our Current Reports on Form 8-K.

Use of Proceeds from Registered Securities

Not applicable.

Purchases of Equity Securities by the Issuer

None.

Item 6. [Reserved.]

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

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

Overview

We are a pharmaceutical company dedicated to maximizing the commercial potential of ORLYNVAH™, the first oral branded penem available in the United States and 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 developed sulopenem in an oral tablet formulation, sulopenem etzadroxil-probenecid, which we refer to herein as oral sulopenem or ORLYNVAH™, as the context so requires. We refer to sulopenem delivered intravenously as sulopenem and, sulopenem together with oral sulopenem/ORLYNVAH™, as our sulopenem program. We believe that sulopenem and ORLYNVAH™ 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.

On October 25, 2024, we received approval from the U.S. Food and Drug Administration (FDA) of our New Drug Application (NDA) for ORLYNVAH™ for the treatment of uncomplicated urinary tract infections (uUTIs) in adult women caused by the designated microorganisms *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women with limited or no alternative oral antibacterial treatment options.

After receiving positive data from our Phase 3 clinical trial known as REnewed ASsessment of Sulopenem in uUTIs caused by Resistant Enterobacterales (REASSURE) in January 2024, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing stakeholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating various strategic alternatives. Following receipt of FDA approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been prioritized. In the event our strategic process to sell, license, or otherwise dispose of our rights to ORLYNVAH™ to maximize value for our stakeholders, does not result in any type of transaction, we are considering our options for commercializing ORLYNVAH™ in the United States with a commercial partner and/or on our own with a targeted sales force in the community setting.

Going Concern

Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the success of our strategic process to sell, license, or otherwise dispose of our rights to sulopenem, the successful commercialization of ORLYNVAH™, and/or the successful development and eventual commercialization of sulopenem and/or of oral sulopenem in additional indications, in each case , if approved. As of December 31, 2024, we had an accumulated deficit of $486.1 million. In the event our strategic process to sell, license, or otherwise dispose of our rights to sulopenem does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting, which we expect would result in significant expenses being incurred by us in the future. We may also incur expenses in connection with the further clinical development of IV sulopenem and the clinical development of oral sulopenem in additional indications, the establishment of additional sources for the manufacture of oral sulopenem tablets and, if relevant, IV vials or the in-license or acquisition of additional product candidates . Additionally, we have incurred and expect to incur significant costs associated with operating as a public company, including legal, accounting, investor relations and other expenses.

As a result, we will require additional capital to fund our operations, to continue to develop our sulopenem program and to execute our strategy. Until such time as we can sell, license, or otherwise dispose of our rights to sulopenem, successfully commercialize ORLYNVAH™, or obtain marketing approval for sulopenem or oral sulopenem in additional indications or any future product candidate and generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements, marketing and distribution arrangements or government funding. However, we may be unable to obtain such financing when needed or on acceptable terms.

Because of the numerous risks and uncertainties associated with commercialization of pharmaceuticals, 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.

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. To continue as a going concern, we must secure additional funding to support our current operating plan or significantly delay, scale back or discontinue the development of our sulopenem program and commercialization of ORLYNVAH™ for the treatment of uncomplicated urinary tract infections caused by the designated microorganisms *Escherichia coli, Klebsiella pneumoniae*, or *Proteusmirabilis* in adult women with limited or no alternative oral antibacterial treatment options. As of December 31, 2024, we had cash and cash equivalents of $24.1 million. Based on our available cash resources, we do not believe that our existing cash and cash equivalents will enable us to fund our operating expenses for the next 12 months from the date of filing this Annual Report on Form 10-K. This condition raises substantial doubt about our ability to continue as a going concern. We expect that in order to obtain additional funding we will need to complete additional public or private financings of debt or equity. Although management intends to pursue plans to obtain additional funding to finance its operations, and we have successfully raised capital in the past, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all.

We may also seek to procure additional funds through future arrangements with collaborators, licensees or other third parties, and these arrangements would generally require us to relinquish or encumber rights to some of our product candidates. We may not be able to complete financings or enter into third-party arrangements on acceptable terms, if at all. If we fail to raise capital or enter into such agreements as and when needed, we may be forced to significantly delay, scale back or discontinue the development and commercialization of our sulopenem program, or otherwise change our strategy, which could adversely affect our business prospects, or we may be unable to continue operations.

In addition, we are currently focusing on a strategic process to sell, license or otherwise dispose of our rights to sulopenem with the goal of maximizing value for our shareholders and engaged a financial advisor to assist management and the board in evaluating strategic alternatives. There can be no assurance that any such process will result in any particular action or any transaction being pursued, entered into or consummated, and there is no assurance as to the timing, sequence or outcome of any action or transaction or series of actions or transactions. For more information, refer to "Liquidity and Capital Resources—Funding Requirements" below and Note 1, "—Liquidity and Going Concern" of the Notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Components of Our Results of Operations

Costs and Expenses

Cost of Sales

Cost of sales consist primarily of amortization related to the finite-lived intangible asset recognized in relation to the regulatory milestone payment payable to Pfizer Inc. (Pfizer) upon approval of ORLYNVAH™ by the FDA.

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 and reservation fees;
- 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, including the preparation and support of regulatory filings;
- facilities costs, depreciation, amortization and other expenses, which include rent under operating lease agreements and utilities; and
- payments made in cash, equity securities or other forms of consideration under third-party licensing agreements.

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

General and Administrative Expenses

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

In the event our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we may seek a commercial partner and/or directly commercialize ORLYNVAH™ in the United States with a targeted sales force in the community setting. This would result in a significant increase in payroll and other expenses to support commercial operations.

Interest Expense, Net

Interest expense, net consists of interest accrued and amortization of debt costs with respect to the 6.500% Exchangeable Senior Subordinated Notes due 2025 (Exchangeable Notes), interest accrued with respect to the promissory note issued by Iterum Therapeutics International Limited (ITIL) in the amount of the milestone payment to Pfizer in connection with us electing to defer payment of the milestone payment due to Pfizer for two years until October 25, 2026 (the Pfizer Promissory Note), realized gains and losses on our short-term investments, interest earned on our cash and cash equivalents, which are generally invested in money market accounts and interest earned on our investments in marketable securities. Interest on the Exchangeable Notes was not payable until maturity of the instrument unless exchanged prior to maturity in accordance with the terms of the indenture governing the Exchangeable Notes (Exchangeable Notes Indenture) at which time any accrued and unpaid interest became due and payable. Interest on the Pfizer Promissory Note is compounded daily and is payable on maturity.

Adjustments to Fair Value of Derivatives

Derivative liabilities, which consist of the Limited Recourse Royalty-Linked Subordinated Notes (RLNs) issued in 2020 are revalued at each balance sheet date and the change in fair value during the reporting period is recorded in the consolidated statements of operations as adjustments to fair value of derivatives.

Other (Expense) / Income, Net

Other (expense) / income, net consists of realized and unrealized foreign currency gains and losses incurred in the normal course of business based on movement in the applicable exchange rates and sub-lease income from a sub-lease agreement for a commercial unit (terminated in August 2023).

Provision for Income Taxes

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

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

Critical Accounting Policies and Significant Judgments and Estimates

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

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

Royalty-Linked Notes

On recognition, the RLNs qualified as debt instruments under ASC 470, *Debt*, and were initially recorded at fair value, applying a DCF model, and then subsequently measured at amortized cost. In January 2021, the RLNs were exchange listed, and therefore, derivative accounting has been applied in accordance with ASC 815, *Derivatives and Hedging,* which establishes accounting and reporting standards for derivative instruments, including certain derivative instruments embedded in other financial instruments or contracts which require bifurcation and measurement at fair value for accounting purposes on the balance sheet date. Any liabilities recorded at fair value are revalued at each reporting period with the resulting change in fair value reflected in the consolidated statements of operations as adjustments to fair value of derivatives.

The RLN liability is carried at fair value on the consolidated balance sheets and determined using a DCF analysis. The key inputs and assumptions used in the DCF model at each reporting date include the terms of the indenture governing the RLNs, royalty payments based on estimated sales volumes and the discount rate. These assumptions require significant judgment and any changes could have a material impact in the determination of revaluation of the RLNs at each reporting date.

Results of Operations

Comparison of the Years Ended December 31, 2024 and 2023

The following table summarizes our operating loss and loss before income tax for the years ended December 31, 2024 and 2023:

	Year Ended December 31,		
	2024	2023	Change
	(In thousands)		
Costs and expenses:			
Cost of sales	$ (254)	$ —	$ (254)
Research and development	(10,458)	(39,992)	29,534
General and administrative	(7,984)	(7,476)	(508)
Total operating expenses	$ (18,696)	$ (47,468)	$ 28,772
Operating loss	(18,696)	(47,468)	28,772
Total other (expense) / income	(5,838)	9,710	(15,548)
Loss before income taxes	$ (24,534)	$ (37,758)	$ 13,224

Cost of Sales Expenses

The increase in cost of sales expenses was primarily due to the amortization associated with the regulatory milestone payable to Pfizer upon approval of ORLYNVAH™ which was capitalized on recognition.

Research and Development Expenses

	Year Ended December 31,		
	2024	2023	Change
	(In thousands)		
CRO and other preclinical and clinical trial expenses	$ 3,413	$ 33,017	$ (29,604)
Personnel related (including share-based compensation)	2,461	3,841	(1,380)
Chemistry, manufacturing and control (CMC) related expenses	2,829	1,954	875
Consulting fees	1,755	1,180	575
Total research and development expenses	$ 10,458	$ 39,992	$ (29,534)

The decrease in CRO and other preclinical and clinical trial expenses of $29.6 million was primarily due to a decrease in costs incurred to support our REASSURE clinical trial, which began enrollment in October 2022 and completed enrollment in October 2023. Personnel related expenses decreased by $1.4 million as a result of lower headcount, a decrease in bonus expense and a decrease in share-based compensation. Personnel related expenses for the years ended December 31, 2024 and 2023 included share-based compensation expense of $0.2 million and $0.4 million, respectively. CMC related expenses increased by $0.9 million primarily as a result of manufacturing of API, partially offset by lower facility rent. Consulting fees increased by $0.6 million primarily as a result of an increase in the use of consultants in connection with the resubmission of our NDA for ORLYNVAH™.

General and Administrative Expenses

	Year Ended December 31,		
	2024	2023	Change
	(In thousands)		
Personnel related (including share-based compensation)	$ 3,186	$ 3,618	$ (432)
Facility related and other	2,085	2,531	(446)
Professional and consultant fees	2,713	1,327	1,386
Total general and administrative expenses	$ 7,984	$ 7,476	$ 508

Personnel related expenses decreased by $0.4 million primarily as a result of a decrease in bonus expense and a decrease in share-based compensation. Personnel related expenses for the years ended December 31, 2024 and 2023 included share-based compensation expense of $0.2 million and $0.3 million, respectively. Facility related and other costs decreased by $0.4 million primarily as a result of a decrease in directors' share-based compensation and insurance costs. Facility related and other costs for the years ended December 31, 2024 and 2023 included directors' share-based compensation expense of $0.0 million and $0.1 million, respectively. Professional and consulting fees increased by $1.4 million primarily as a result of an increase in legal fees and an increase in consultants used to support pre-commercial activities.

The following table summarizes our total other (expense) / income for the years ended December 31, 2024 and 2023:

	Year Ended December 31,		
	2024	2023	Change
	(In thousands)		
Interest expense, net	$ (2,522)	$ (1,428)	$ (1,094)
Adjustments to fair value of derivatives	(3,269)	11,056	(14,325)
Other (expense) / income, net	(47)	82	(129)
Total other (expense) / income	$ (5,838)	$ 9,710	$ (15,548)

Interest Expense, Net

Interest expense, net increased by $1.1 million for the year ended December 31, 2024 primarily as a result of a decrease in interest income on short-term investments and money market funds and interest accruing on the Pfizer Promissory Note.

Adjustments to Fair Value of Derivatives

Adjustments to the fair value of the derivative liability were $3.3 million for the year ended December 31, 2024. This non-cash adjustment primarily related to an increase in the fair value of the RLNs upon regulatory approval of ORLYNVAH™ and due to the passage of time.

Adjustments to the fair value of the derivative liability were $11.1 million for the year ended December 31, 2023. This non-cash adjustment related to a decrease in fair value of the RLNs due to a reduction in management's revenue forecast of U.S. sulopenem sales.

Other (Expense) / Income, Net

Other (expense) / income, net consists of realized and unrealized foreign currency gains and losses incurred in the normal course of business based on movement in the applicable exchange rates and sub-lease income from a sub-lease agreement for a commercial unit (which was terminated on August 31, 2023). The decrease of $0.1 million is primarily related to a decrease in sublease income.

Comparison of the Years Ended December 31, 2023 and 2022

The following table summarizes our operating loss and loss before tax for the years ended December 31, 2023 and 2022:

	Year Ended December 31,		
	2023	2022	Change
	(In thousands)		
Costs and expenses:			
Research and development	$ (39,992)	$ (17,617)	$ (22,375)
General and administrative	(7,476)	(12,766)	5,290
Total operating expenses	$ (47,468)	$ (30,383)	$ (17,085)
Operating loss	(47,468)	(30,383)	(17,085)
Total other expense	9,710	(13,750)	23,460
Loss before income taxes	$ (37,758)	$ (44,133)	$ 6,375

Research and Development Expenses

	Year Ended December 31,		
	2023	2022	Change
	(In thousands)		
CRO and other preclinical and clinical trial expenses	$ 33,017	$ 9,374	$ 23,643
Personnel related (including share-based compensation)	3,841	4,446	(605)
Chemistry, manufacturing and control (CMC) related expenses	1,954	2,642	(688)
Consulting fees	1,180	1,155	25
Total research and development expenses	$ 39,992	$ 17,617	$ 22,375

The increase in CRO and other preclinical and clinical trial expenses of $23.6 million was primarily due to an increase in costs incurred to support our REASSURE clinical trial, which began enrollment in October 2022 and completed enrollment in October 2023. Personnel related expenses decreased by $0.6 million as a result of a decrease in share-based compensation, partially offset by an increase in employee compensation. Personnel related expenses for the years ended December 31, 2023 and 2022 included share-based compensation expense of $0.4 million and $1.4 million, respectively. CMC related expenses decreased by $0.7 million primarily due to the write-off of a valuation allowance held against a research and development tax credit, partially offset by an increase in activities related to our REASSURE clinical trial. Consulting fees of $1.2 million were substantially the same as those incurred in the prior year.

General and Administrative Expenses

	Year Ended December 31,		
	2023	2022	Change
	(In thousands)		
Personnel related (including share-based compensation)	$ 3,618	$ 6,153	$ (2,535)
Facility related and other	2,531	3,527	(996)
Professional and consultant fees	1,327	3,086	(1,759)
Total general and administrative expenses	$ 7,476	$ 12,766	$ (5,290)

Personnel related expenses decreased by $2.5 million primarily as a result of a decrease in share-based compensation. Personnel related expenses for the years ended December 31, 2023 and 2022 included share-based compensation expense of $0.3 million and $2.8 million, respectively. Facility related and other costs decreased by $1.0 million primarily as a result of a decrease in directors' fees, directors' share-based compensation, insurance costs and rent expense. Facility related and other costs for the years ended December 31, 2023 and 2022 included directors' share-based compensation expense of $0.1 million and $0.6 million, respectively. Professional and consulting fees decreased by $1.8 million primarily as a result of a decrease in legal fees associated with the lawsuit filed in August 2021 which was dismissed with prejudice in January 2023.

The following table summarizes our total other income / (expense) for the years ended December 31, 2023 and 2022:

	Year Ended December 31,		
	2023	2022	Change
	(In thousands)		
Interest expense, net	$ (1,428)	$ (2,361)	$ 933
Adjustments to fair value of derivatives	11,056	5,458	5,598
Cancellation of share options	—	(17,350)	17,350
Other income, net	82	503	(421)
Total other income / (expense)	$ 9,710	$ (13,750)	$ 23,460

Interest Expense, Net

Interest expense, net decreased by $0.9 million for the year ended December 31, 2023 primarily as a result of higher interest income on short-term investments and money market funds and lower unrealized losses on short-term investments.

Adjustments to Fair Value of Derivatives

Adjustments to the fair value of the derivative liability were $11.1 million and $5.5 million for the years ended December 31, 2023 and 2022, respectively. This non-cash adjustment in 2023 related to a decrease in fair value of the RLNs due to a reduction in management's revenue forecast of U.S. sulopenem sales. This non-cash adjustment in 2022 primarily related to a decrease in the value of derivative components associated with the Exchangeable Notes due to the decrease in our market value.

Cancellation of Share Options

On July 7, 2022, certain of our executive officers and employees agreed to the surrender and cancellation of certain previously granted share options in order to make available additional shares under our Amended and Restated 2018 Equity Incentive Plan. Total expense recognized in connection with the cancellation of these employee share options was $17.4 million for the year ended December 31, 2022.

Other Income, Net

Other income, net consists of realized and unrealized foreign currency gains and losses incurred in the normal course of business based on movement in the applicable exchange rates and sub-lease income from a sub-lease agreement for a commercial unit. The decrease of $0.4 million is primarily related to a reduction in foreign currency gains and a decrease in sublease income. The sub-lease agreement terminated on August 31, 2023.

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 the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) program. We have funded our operations to date primarily through the issuance of ordinary and convertible preferred shares, warrants, debt raised under financing arrangements with SVB including the PPP loan, a sub-award from the Trustees of Boston University under the CARB-X program and the proceeds of the private placement which closed in January 2020 (the Private Placement) and the subsequent rights offering (the 2020 Rights Offering) pursuant to which our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), issued and sold $51.8 million aggregate principal amount of Exchangeable Notes and $0.1 million aggregate principal amount of RLNs. Through December 31, 2024, we had received cash proceeds of $198.3 million from sales of our Series A and Series B preferred shares and ordinary shares, $15.0 million from the first drawdown of our SVB loan, net proceeds of $45.0 million from the Private Placement and the 2020 Rights Offering, $0.7 million from the drawdown of our PPP loan, combined net proceeds of $8.6 million from the registered direct offering in June 2020 (June 3, 2020 Offering) and the registered direct offering in June 2020 (June 30, 2020 Offering) and $1.8 million from the exercise of warrants issued in the June 30, 2020 Offering, net proceeds of $15.5 million from the underwritten offering in October 2020 (October 2020 Offering) and $13.9 million from the exercise of warrants issued in the October 2020 Offering, net proceeds of $42.1 million from the underwritten offering in February 2021 (February 2021 Underwritten Offering) and $0.5 million from the exercise of warrants issued in the February 2021 Underwritten Offering, net proceeds of $32.2 million from the registered direct offering in February 2021 (February 2021 Registered Direct Offering), net proceeds of $5.4 million from the 2024 Rights Offering (2024 Rights Offering) and $1.0 million from the exercise of 1-year warrants issued in the 2024 Rights Offering and $0.8 million from the exercise of 5-year warrants issued in the 2024 Rights Offering.

On October 7, 2022, we filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on October 17, 2022 (File No. 333-267795), and pursuant to which we registered for sale up to $100.0 million of any combination of debt securities, ordinary shares, preferred shares, subscription rights, purchase contracts, units and/or warrants from time to time and at prices and on terms that we may determine. On October 7, 2022, we entered into an “at the market offering” agreement (the Sales Agreement), with H.C. Wainwright & Co., LLC (HC Wainwright), as agent, pursuant to which we could offer and sell ordinary shares, nominal value $0.01 per share (the ordinary shares) for aggregate gross sales proceeds of up to $16.0 million (subject to the availability of ordinary shares), from time to time through HC Wainwright by any method permitted that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended (the Securities Act). On December 10, 2024, we filed a prospectus supplement with the Securities and Exchange Commission (SEC) pursuant to which we may offer and sell ordinary shares having an aggregate offering price of up to an additional $25.0 million through HC Wainwright pursuant to the Sales Agreement.

During the year ended December 31, 2024, we sold 10,327,787 ordinary shares under the Sales Agreement at an average price of $1.94 per share for net proceeds of $19.4 million, after deducting commissions to HC Wainwright of $0.6 million.

As of December 31, 2024, we had cash and cash equivalents of $24.1 million.

2025 Exchangeable Notes and Royalty-Linked Notes

On January 21, 2020, we completed the Private Placement pursuant to which our wholly owned subsidiary, Iterum Bermuda issued and sold $51.6 million aggregate principal amount of Exchangeable Notes and $0.1 million aggregate principal amount of RLNs, to a group of accredited investors. On September 8, 2020, we completed the Rights Offering pursuant to which Iterum Bermuda issued and sold $0.2 million aggregate principal amount of Exchangeable Notes and $0.04 million aggregate principal amount of RLNs, to existing shareholders. The Exchangeable Notes and RLNs were sold in Units with each Unit consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs. The Units were sold at a price of $1,000 per Unit. At any time on or after January 21, 2021, subject to specified limitations, the Exchangeable Notes were exchangeable for our ordinary shares, cash or a combination of ordinary shares and cash, at an exchange rate of 191.7028 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an exchange price of approximately 5.2164 per ordinary share) as of December 31, 2024, which exchange rate was adjusted from an initial exchange rate of 66.666 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $15.00 per ordinary share), and were subject to further adjustment pursuant to the terms of the Exchangeable Notes Indenture. The Exchangeable Notes matured on January 31, 2025. Beginning on January 21, 2021 to December 31, 2024, certain noteholders of $40,691 aggregate principal amount of Exchangeable Notes have exchanged their notes for an aggregate of 3,760,155 of our ordinary shares, which included accrued and unpaid interest relating to such notes. The aggregate principal amount of Exchangeable Notes outstanding as of December 31, 2024 was $11.1 million. We repaid the aggregate principal and accrued and unpaid interest in full on January 31, 2025. The RLNs entitle holders to payments based on a percentage of our net revenues from potential U.S. sales of specified sulopenem products subject to the terms and conditions of the indenture governing the RLNs (the RLN Indenture). Pursuant to the RLN Indenture, the payments on the RLNs will be 15% of net revenues from U.S. sales of such products. The aggregate amount of payments on each RLN is capped at $160.00 (or 4,000 times the principal amount of such RLN). Iterum Bermuda received net proceeds from the sale of the Units of $45.0 million, after deducting placement agent fees and offering expenses.

Registered Direct Offerings

On June 3, 2020, we entered into the securities purchase agreement (June 3, 2020 SPA) with certain institutional investors pursuant to which we issued and sold, in the June 3, 2020 Offering, an aggregate of 198,118 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $25.2375, for aggregate gross proceeds to us of $5.0 million and net proceeds of $4.3 million after deducting fees payable to the placement agent and other offering expenses payable by us. We offered the ordinary shares in the June 3, 2020 Offering pursuant to our universal shelf registration statement on Form S-3, which was declared effective on July 16, 2019 (File No. 333-232569) (the 2019 Shelf Registration Statement). Pursuant to the June 3, 2020 SPA, in a concurrent private placement, we issued and sold to the June 3 Purchasers warrants to purchase up to 99,057 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $24.30 per ordinary share, subject to adjustment in certain circumstances, and will expire on December 5, 2025. The closing date of the June 3, 2020 Offering was June 5, 2020. Warrants to purchase 13,868 ordinary shares, amounting to 7% of the ordinary shares issued under the June 3, 2020 SPA, were issued to designees of the placement agent on the closing of the June 3, 2020 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $31.5465 per ordinary share, and will expire on June 3, 2025.

On June 30, 2020, we entered into the securities purchase agreement (June 30, 2020 SPA) with certain institutional investors pursuant to which we issued and sold in the June 30, 2020 Offering an aggregate of 224,845 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $22.2375, for aggregate gross proceeds to us of $5.0 million and net proceeds of $4.2 million after deducting fees payable to the placement agent and other offering expenses payable by us. We offered the ordinary shares in the June 30, 2020 Offering pursuant to the 2019 Shelf Registration Statement. Pursuant to the June 30, 2020 SPA, in a concurrent private placement, we issued and sold to the June 30 Purchasers warrants to purchase up to 112,422 ordinary shares. Upon closing, the warrants were exercisable immediately at an exercise price of $21.30 per ordinary share, subject to adjustment in certain circumstances, and will expire on January 2, 2026. The June 30, 2020 Offering closed on July 2, 2020. Warrants to purchase 15,739 ordinary shares, amounting to 7% of the ordinary shares issued under the June 30, 2020 SPA, were issued to designees of the placement agent on closing of the June 30, 2020 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $27.7965 per ordinary share, and will expire on June 30, 2025.

On February 9, 2021, we entered into the securities purchase agreement (February SPA) with certain institutional investors pursuant to which we issued and sold in the February 2021 Registered Direct Offering an aggregate of 1,166,666 ordinary shares, $0.01 nominal value per share, at a purchase price of $30.00 per share, for aggregate net proceeds to us of $32.2 million after deducting placement agent fees and other offering expenses payable by us. We offered the ordinary shares in the February 2021 Registered Direct Offering pursuant to the 2019 Shelf Registration Statement. The February 2021 Registered Direct Offering closed on February 12, 2021. Warrants to purchase 81,666 ordinary shares, amounting to 7.0% of the aggregate number of ordinary shares issued under the February SPA, were issued to designees of the placement agent on closing of the February 2021 Registered Direct Offering. Upon closing, warrants issued to such designees became exercisable immediately at an exercise price of $37.50 per ordinary share and will expire on February 9, 2026.

October 2020 Offering

On October 27, 2020, we completed the October 2020 Offering in which we sold an aggregate of (i) 1,034,102 ordinary shares, $0.01 nominal value per share, (ii) pre-funded warrants exercisable for an aggregate of 760,769 ordinary shares and (iii) warrants exercisable for an aggregate of 1,346,153 ordinary shares. The pre-funded warrants were issued and sold to certain purchasers whose purchase of ordinary shares in the October 2020 Offering would have otherwise resulted in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% (or, at the election of the purchaser, 9.99%) of our outstanding ordinary shares immediately following the consummation of the October 2020 Offering, if the purchaser so chose in lieu of ordinary shares that would have otherwise resulted in such excess ownership. The ordinary shares and pre-funded warrants were each offered together with the warrants, but the ordinary shares and pre-funded warrants were issued separately from the warrants. The combined offering price was $9.75 per ordinary share and warrant and $9.60 per pre-funded warrant and warrant. Our net proceeds from the October 2020 Offering, after deducting placement agent fees and other offering expenses payable by us, were approximately $15.5 million. The warrants are exercisable upon issuance at a price of $9.75 per ordinary share, subject to adjustment in certain circumstances, and expire on October 27, 2025. The pre-funded warrants are exercisable upon issuance at a price of $0.15 per ordinary share, subject to adjustment in certain circumstances, and expire when exercised in full, subject to certain conditions. All pre-funded warrants have been exercised for net proceeds of $0.11 million. In connection with the October 2020 Offering, we entered into a Purchase Agreement on October 22, 2020 with certain institutional investors. The Purchase Agreement contains customary representations and warranties of ours, termination rights of the parties, and certain indemnification obligations of ours. Warrants to purchase 125,641 ordinary shares, which represents a number of ordinary shares equal to 7.0% of the aggregate number of ordinary shares and pre-funded warrants sold in the October 2020 Offering, were issued to designees of the placement agent on closing of the October 2020 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $12.1875 per ordinary share and will expire on October 22, 2025.

February 2021 Underwritten Offering

On February 3, 2021, we entered into an underwriting agreement (the Underwriting Agreement) pursuant to which we issued and sold 2,318,840 ordinary shares, $0.01 nominal value per share, at a public offering price of $17.25 per share. We offered the ordinary shares in the February 2021 Underwritten Offering pursuant to the 2019 Shelf Registration Statement. The February 2021 Underwritten Offering closed on February 8, 2021. Pursuant to the Underwriting Agreement, we granted the underwriter an option for a period of 30 days to purchase up to an additional 347,826 ordinary shares on the same terms and conditions, which the underwriter exercised in full on February 10, 2021. This increased the total number of ordinary shares we sold in the February 2021 Underwritten Offering to 2,666,666 shares, which resulted in aggregate net proceeds of $42.1 million after deducting underwriting discounts and commissions and offering expenses. In addition, pursuant to the Underwriting Agreement, we agreed to issue to the underwriter's designees warrants to purchase 186,665 ordinary shares, which is equal to 7.0% of the aggregate number of ordinary shares sold in the February 2021 Underwritten Offering, including the underwriter's option to purchase an additional 347,826 ordinary shares. The warrants issued to such designees of the underwriter have an exercise price of $21.5625 per ordinary share, were exercisable upon issuance and will expire on February 3, 2026.

2024 Rights Offering

On August 9, 2024, we completed the 2024 Rights Offering in which we sold an aggregate of 6,121,965 units (Units) at a subscription price of $1.21 per whole Unit, consisting of (a) one ordinary share, (b) a warrant to purchase 0.50 ordinary shares, at an exercise price of $1.21 per whole ordinary share from the date of issuance through its expiration one year from the date of issuance (1-year warrants) and (c) a warrant to purchase one ordinary share, at an exercise price of $1.21 per whole ordinary share from the date of issuance through its expiration five years from the date of issuance (the 5-year warrants and, together with the 1-year warrants, the warrants). Our net proceeds from the 2024 Rights Offering, after deducting dealer-manager fees and other offering expenses payable by us, were approximately $5.4 million. The warrants are exercisable upon issuance at a price of $1.21 per ordinary share and the 1-year warrant will expire on August 9, 2025 and the 5-year warrants will expire on August 9, 2029.

Cash Flows

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

	Year Ended December 31,		
	2024	2023	2022
	(In thousands)		
Net cash used in operating activities	$ (26,770)	$ (39,330)	$ (18,473)
Net cash provided by investing activities	18,208	23,336	13,957
Net cash provided by / (used in) financing activities	26,691	1,034	(1,818)
Effect of exchange rates on cash and cash equivalents	(75)	(61)	(50)
Net increase / (decrease) in cash, cash equivalents and restricted cash	$ 18,054	$ (15,021)	$ (6,384)

Operating Activities

During the year ended December 31, 2024, operating activities used $26.8 million of cash, resulting from our net loss of $24.8 million and net cash used by changes in our operating assets and liabilities of $12.7 million, partially offset by non-cash adjustments of $10.7 million. Net cash used by changes in our operating assets and liabilities for the year ended December 31, 2024 consisted primarily of a decrease in accounts payable and accrued expenses primarily due to a reduction in costs due to the completion of our REASSURE clinical trial, partially offset by a decrease in prepaid expenses and other current assets.

During the year ended December 31, 2023, operating activities used $39.3 million of cash, resulting from our net loss of $38.4 million and non-cash adjustments of $3.7 million, partially offset by net cash provided by changes in our operating assets and liabilities of $2.8 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2023 consisted primarily of an increase in accounts payable and accrued expenses, partially offset by an increase in prepaid expenses and other current assets.

During the year ended December 31, 2022, operating activities used $18.5 million of cash, resulting from our net loss of $44.4 million, partially offset by non-cash charges of $23.7 million, consisting primarily of $17.4 million of expense for the cancellation of share options, and net cash provided by changes in our operating assets and liabilities of $2.3 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2022 consisted primarily of an increase in accounts payable and accrued expenses.

Investing Activities

During the year ended December 31, 2024, net cash provided by investing activities was primarily related to sales of short-term investments of $30.6 million, partially offset by purchases of short-term investments of $12.4 million. During the year ended December 31, 2023, net cash provided by investing activities was primarily related to sales of short-term investments of $64.5 million, partially offset by purchases of short-term investments of $41.2 million. During the year ended December 31, 2022, net cash provided by investing activities was primarily related to sales of short-term investments of $59.7 million, partially offset by purchases of short-term investments of $45.7 million.

Financing Activities

During the year ended December 31, 2024, net cash provided by financing activities of $26.7 million was related to net proceeds from the sale of ordinary shares of $19.4 million pursuant to the Sales Agreement, net proceeds from the sales of ordinary shares in the 2024 Rights Offering of $5.4 million, proceeds from the exercise of warrants in connection with the 2024 Rights Offering of $1.8 million and proceeds from the exercise of share options of $0.1 million. During the year ended December 31, 2023, net cash provided by financing activities of $1.0 million was related to net proceeds from the sale of ordinary shares of $1.0 million pursuant to the Sales Agreement. During the year ended December 31, 2022, net cash used in financing activities of $1.8 million was related to principal repayments made to SVB under the Loan and Security Agreement, including a final payment fee, and the PPP loan, partially offset by net proceeds from the sale of ordinary shares of $0.4 million pursuant to the Sales Agreement.

Funding Requirements

After receiving positive data from our REASSURE trial in January 2024, our board of directors determined that we should focus on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing shareholder value. In connection with this strategic process, we engaged a financial advisor to assist management and the board in evaluating strategic alternatives. Following receipt of FDA approval for ORLYNVAH™ in October 2024, efforts to achieve a strategic transaction have been renewed. In the event that our strategic process does not result in any type of transaction, and subject to our ability to raise sufficient capital to fund operations, we expect to continue to incur significant expenses and increasing operating losses as we prepare to commercialize ORLYNVAH™.

As of December 31, 2024, we had cash and cash equivalents of $24.1 million. Our expected cash usage for the next 12 months assumes that planned programs and expenditure continue and that we do not reduce or eliminate some or all of our research and development programs or commercialization efforts. Our future viability is dependent on our ability to raise additional capital to finance our operations. Without additional external funding, we do not believe that our existing cash and cash equivalents will enable us to fund our operating expenses for the next 12 months from the date of this Annual Report on Form 10-K. As such, we believe this condition raises substantial doubt about our ability to continue as a going concern for at least one year from the date this Annual Report on Form 10-K is filed with the SEC.

Inflation generally affects us by increasing our cost of labor and certain services. We do not believe that inflation had a material effect on our financial statements included elsewhere in this Annual Report on Form 10-K. However, the United States has recently experienced historically high levels of inflation. If the inflation rate continues to increase it may affect our expenses, such as employee compensation and research and development charges due to, for example, increases in the costs of labor and supplies. Additionally,

the United States is experiencing a workforce shortage, which in turn has created a competitive wage environment that may also increase our operating costs in the future.

Our expenses will also increase substantially if and as we:

•initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates;

•establish sales, marketing and distribution capabilities either directly or through a third-party, to commercialize ORLYNVAH™ in the United States;

•establish sales, marketing and distribution capabilities either directly or through a third-party, to commercialize oral sulopenem in additional indications, and/or future product candidates in the United States, if we obtain marketing approval from the FDA;

•establish manufacturing and supply chain capacity sufficient to provide commercial quantities of ORLYNVAH™ in additional indications, and/or future product candidates, if we obtain marketing approval, and undertake commercialization activities;

•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; and

•acquire or in-license other product candidates or technologies.

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

•the costs of commercialization activities for ORLYNVAH™, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;

•the costs of commercialization activities for ORLYNVAH™ in additional indications and any 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 revenue received from any potential commercial sales of ORLYNVAH™;

•the receipt of marketing approval and revenue received from any potential commercial sales of ORLYNVAH™ in additional indications or future product candidates;

•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 amount and timing of any payments we may be required to make in connection with the RLNs;

•the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;

•the timing and costs of our clinical trials of our product candidates, including any clinical trials or non-clinical studies which may be required for regulatory approval of our product candidates;

•the timing of regulatory review and potential approval of any product candidates;

•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 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 operating as a public company;

•the extent to which we in-license or acquire other products and technologies;

•the impact of general economic conditions, including inflation; and

•the outcome, impact, effects and results of our evaluation of corporate, strategic, financial and financing alternatives, including the terms, timing, structure, value, benefits and costs of any corporate, strategic, financial or financing alternative and our ability to complete one at all.

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. The disruption and volatility in the global and domestic capital markets resulting from heightened inflation, capital market volatility, interest rate and currency rate fluctuations, artificial intelligence, regulatory changes under the new Trump Administration, any potential economic slowdown or recession, including trade wars or civil or political unrest (such as the ongoing war between Ukraine and Russia, conflict in the Middle East, and tension between China and Taiwan) may increase the cost of capital and limit our ability to access capital. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our shareholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our ordinary shareholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. The RLNs and the investor rights agreement we entered into in connection with the Private Placement each impose operating and other restrictions on us. Such restrictions affect, and in many cases limit or prohibit, our ability to dispose of certain assets, pay dividends, incur additional indebtedness, undergo a change of control and enter into certain collaborations, strategic alliances or other similar partnerships, among other things. If we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves. In addition, as described above, we are evaluating our corporate, strategic, financial and financing alternatives, with the goal of maximizing value for our shareholders while prudently managing our resources.

Contractual Obligations and Commitments

Under the Pfizer License, we have agreed to make certain regulatory and sales milestone payments. We are obligated to make a potential one-time payment related to sublicensing income that exceeds a certain threshold. We are also obligated to pay Pfizer sales milestones upon achievement of net sales ranging from $250.0 million to $1.0 billion for each product type, as well as royalties ranging from a single-digit to mid-teens percentage based on marginal net sales of each licensed product.

Under the RLN Indenture, holders of RLNs will be entitled to payments based solely on a percentage of our net revenues from U.S. sales of specified sulopenem products (Specified Net Revenues). Payments will be due within 75 days of the end of each six-month payment measuring period (Payment Measuring Period), beginning with the Payment Measuring Period ending June 30, 2020 until (i) the "Maximum Return" (as described below) has been paid in respect of the RLNs, or (ii) the "End Date" occurs, which is December 31, 2045, or (iii) December 31, 2025, in the event that we have not yet received FDA approval with respect to one or more specified sulopenem products by such date. The aggregate amount of payments in respect of all RLNs during each Payment Measuring Period will be equal to the product of total Specified Net Revenues earned during such period and the applicable payment rate (the Payment Rate), being 15%. There was no payment due for each of the Payment Measuring Periods through the payment measuring period ending December 31, 2024. Prior to the End Date, we are obligated to make payments on the RLNs from Specified Net Revenues until each RLN has received payments equal to $160.00 (or 4,000 times the principal amount of such RLN) (Maximum Return).

Our operating lease obligations primarily consist of payments for office space, which are described further in Note 8 of our consolidated financial statements included in this Annual Report on Form 10-K. Future contractual payments on operating lease obligations due within one year of December 31, 2024 are $0.1 million, and there were no future contractual payments on operating lease obligations due greater than one year from December 31, 2024.

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 SEC.

Recently Issued Accounting Pronouncements

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

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

As of December 31, 2024, we had cash and cash equivalents of $24.1 million, consisting primarily of cash and investments in money market funds. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk.

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, 2024 and 2023, substantially all of our liabilities were denominated in U.S. dollars. Realized net foreign currency gains and losses did not have a material effect on our results of operations for the years ended December 31, 2024 and 2023. We do not currently engage in any hedging activities against our foreign currency exchange rate risk.

Inflation generally affects us by increasing our cost of labor and research, manufacturing and development costs. We believe that inflation has not had a material effect on our financial statements included elsewhere in this Annual Report on Form 10-K. However, our operations may be adversely affected by inflation in the future.

Item 8. Financial Statements and Supplementary Data.

ITERUM THERAPEUTICS PLC

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm (KPMG, Dublin, Ireland, Auditor Firm ID: 1116)	116
Consolidated Balance Sheets	118
Consolidated Statements of Operations and Comprehensive Loss	119
Consolidated Statements of Shareholders' Equity / (Deficit)	120
Consolidated Statements of Cash Flows	121
Notes to Consolidated Financial Statements	122

Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors
Iterum Therapeutics plc:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Iterum Therapeutics plc and subsidiaries (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, shareholders' equity/(deficit), and cash flows for each of the years in the three-year period ended December 31, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

Going Concern

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

Basis for Opinion

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

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

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the (consolidated) financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Measurement of Royalty Linked Notes liability

As discussed in Notes 2 and 11 to the consolidated financial statements, the carrying amount of the Royalty-Linked Notes (RLN) which originated from the 2020 Private Placement amounted to $10.8 million as of December 31, 2024. The RLN liability is carried at fair value on the consolidated balance sheet and determined using a discounted cash flow (DCF) analysis.

We identified the evaluation of the fair value of the RLN liability as a critical audit matter. Subjective auditor judgment was required in assessing the discount rate and estimated sales volume assumptions used in the DCF analysis to estimate the fair value of the

RLN. Minor changes to these assumptions would have a material impact on the estimated fair value. Additionally, specialized skills and knowledge were needed to evaluate the discount rate.

The following are the primary procedures we performed to address this critical audit matter:

- We evaluated the design of a certain internal control related to the estimation of the RLN liability.
- We evaluated the reasonableness of the estimated sales volume assumptions by comparing them to (1) company-specific operational information and management's communication to the Board of Directors and (2) available industry or other third-party reports on expected market opportunities.
- We involved valuation professionals with specialized skills and knowledge, who assisted in evaluating the discount rates by comparing them against the ranges that were independently developed using publicly available market data of comparable entities.
- We performed sensitivity analyses on the fair value of the RLN liability based on changes to the discount rate.

s/ KPMG

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

Dublin, Ireland
February 7, 2025

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

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 24,125	$ 6,071
Short-term investments	—	17,859
Prepaid expenses and other current assets	614	1,628
Income taxes receivable	48	38
Total current assets	24,787	25,596
Intangible asset, net	19,746	—
Property and equipment, net	23	51
Restricted cash	34	34
Other assets	5	578
Total assets	$ 44,595	$ 26,259
Liabilities and Shareholders' Deficit		
Current liabilities:		
Accounts payable	$ 251	$ 4,996
Accrued expenses	2,651	7,761
Exchangeable notes	14,463	—
Other current liabilities	240	761
Total current liabilities	17,605	13,518
Long-term debt - Exchangeable notes	—	11,453
Long-term debt - Pfizer Promissory Note	20,300	—
Royalty-linked notes	10,771	7,503
Other liabilities	—	188
Total liabilities	$ 48,676	$ 32,662
Commitments and contingencies *(Note 16)*		
Shareholders' deficit		
Undesignated preferred shares, $0.01 par value per share: 100,000,000 shares authorized at December 31, 2024 and December 31, 2023; no shares issued at December 31, 2024 and December 31, 2023	—	—
Ordinary shares, $0.01 par value per share: 80,000,000 shares authorized at December 31, 2024 and December 31, 2023, 31,534,233 shares issued at December 31, 2024; 13,499,003 shares issued at December 31, 2023	315	135
Additional paid-in capital	481,676	454,759
Accumulated deficit	(486,072)	(461,298)
Accumulated other comprehensive gain	—	1
Total shareholders' deficit	(4,081)	(6,403)
Total liabilities and shareholders' deficit	$ 44,595	$ 26,259

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

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

	Year ended December 31,		
	2024	**2023**	**2022**
Costs and expenses:			
Cost of sales	$ (254)	$ —	$ —
Research and development	(10,458)	(39,992)	(17,617)
General and administrative	(7,984)	(7,476)	(12,766)
Total operating expenses	(18,696)	(47,468)	(30,383)
Operating loss	(18,696)	(47,468)	(30,383)
Interest expense, net	(2,522)	(1,428)	(2,361)
Adjustments to fair value of derivatives	(3,269)	11,056	5,458
Cancellation of share options	—	—	(17,350)
Other (expense) / income, net	(47)	82	503
Total other (expense) / income	(5,838)	9,710	(13,750)
Loss before income taxes	(24,534)	(37,758)	(44,133)
Income tax expense	(240)	(613)	(301)
Net loss	$ (24,774)	$ (38,371)	$ (44,434)
Net loss per share – basic and diluted	$ (1.26)	$ (2.96)	$ (3.63)
Weighted average ordinary shares outstanding – basic and diluted	19,699,260	12,962,362	12,236,607
Statements of Comprehensive Loss			
Net loss	$ (24,774)	$ (38,371)	$ (44,434)
Other comprehensive (loss) / income:			
Unrealized (loss) / income on marketable securities	(1)	351	(350)
Comprehensive loss	$ (24,775)	$ (38,020)	$ (44,784)

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

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

	Ordinary Shares		Additional Paid in Capital	Accumulated Deficit	Accumulated Other Comprehensive Gain / (Loss)	Total
	Shares	Amount				
Balance at December 31, 2021	12,185,019	$ 122	$ 428,605	$ (378,493)	$ —	50,234
Issuance of ordinary shares, net	413,622	4	437	—	—	441
Share-based compensation expense	—	—	4,758	—	—	4,758
Cancellation of share options	—	—	17,350	—	—	17,350
Net loss	—	—	—	(44,434)		(44,434)
Unrealized loss on available-for-sale securities	—	—	—	—	(350)	(350)
Balance at December 31, 2022	12,598,641	$ 126	$ 451,150	$ (422,927)	$ (350)	27,999
Issuance of ordinary shares, net	732,763	7	1,027	—	—	1,034
Issuance of ordinary shares on conversion of exchangeable notes	167,599	2	1,798	—	—	1,800
Share-based compensation expense	—	—	784	—	—	784
Net loss	—	—	—	(38,371)	—	(38,371)
Unrealized income on available-for-sale securities	—	—	—	—	351	351
Balance at December 31, 2023	13,499,003	$ 135	$ 454,759	$ (461,298)	$ 1	(6,403)
Issuance of ordinary shares, net	16,449,752	164	21,953	—	—	22,117
Issuance of warrants for ordinary shares, net	—	—	2,718	—	—	2,718
Exercise of warrants for ordinary shares	1,498,145	15	1,797	—	—	1,812
Exercise of share options	87,333	1	86	—	—	87
Share-based compensation expense	—	—	363	—	—	363
Net loss	—	—	—	(24,774)	—	(24,774)
Unrealized loss on available-for-sale securities	—	—	—	—	(1)	(1)
Balance at December 31, 2024	31,534,233	$ 315	$ 481,676	$ (486,072)	$ —	(4,081)

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

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

	Year ended December 31,		
	2024	2023	2022
Cash flows from operating activities:			
Net loss	$ (24,774)	$ (38,371)	$ (44,434)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation	30	31	84
Amortization	254	1,719	1,716
Lease termination adjustments	—	473	—
Share-based compensation expense	363	784	4,758
Cancellation of share options expense	—	—	17,350
Amortization of short-term investments	(352)	(1,145)	(183)
Interest on short-term investments	1	55	(55)
Amortization of debt discount and deferred financing costs	2,288	2,339	2,338
Interest on exchangeable notes - non-cash	723	811	819
Interest on promissory note - non-cash	300	—	—
Adjustments to fair value of derivatives	3,269	(11,056)	(5,458)
Other	3,859	2,267	2,281
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(2,663)	(3,188)	(1,551)
Other assets	17	322	—
Accounts payable	(4,745)	2,223	1,895
Accrued expenses	(5,110)	3,489	3,185
Income taxes	155	271	(510)
Other liabilities	(385)	(354)	(708)
Net cash used in operating activities	(26,770)	(39,330)	(18,473)
Cash flows from investing activities:			
Purchases of property and equipment	(2)	(13)	(62)
Purchases of short-term investments	(12,390)	(41,179)	(45,708)
Proceeds from sale of short-term investments	30,600	64,528	59,727
Net cash provided by investing activities	18,208	23,336	13,957
Cash flows from financing activities:			
Repayments of long-term bank debt	—	—	(2,251)
Proceeds from issuance of ordinary shares, net of transaction costs	26,691	1,034	433
Net cash provided by / (used in) financing activities	26,691	1,034	(1,818)
Effect of exchange rates on cash and cash equivalents	(75)	(61)	(50)
Net increase / (decrease) in cash, cash equivalents and restricted cash	18,054	(15,021)	(6,384)
Cash, cash equivalents and restricted cash, at beginning of period	6,105	21,126	27,510
Cash, cash equivalents and restricted cash, at end of period	$ 24,159	$ 6,105	$ 21,126
Supplemental Disclosure of Cash Flow Information:			
Income tax paid—U.S.	$ 220	$ 401	$ 821
Interest paid	—	—	22
Non-cash proceeds — Pfizer Promissory Note	20,000	—	—

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

(1)Nature of Operations and Basis of Presentation

Description of Business

Iterum Therapeutics plc (the Company) was incorporated under the laws of the Republic of Ireland in June 2015 as a limited company and re-registered as a public limited company on March 20, 2018. The Company maintains its registered office at 3 Dublin Landings, North Wall Quay, Dublin 1, D01 C4E0, 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 dedicated to maximizing the commercial potential of ORLYNVAH™, the first oral branded penem available in the United States and potentially the first and only oral and intravenous (IV) branded penem available globally. The Company has developed sulopenem in an oral tablet formulation, sulopenem etzadroxil-probenecid, which is referred to herein as oral sulopenem or ORLYNVAH™, as the context so requires, and is advancing the development of an IV formulation. The Company refers to sulopenem delivered intravenously as sulopenem and, sulopenem together with oral sulopenem/ORLYNVAH™, as its sulopenem program.

Liquidity and Going Concern

Since inception, the Company has devoted substantially all of its efforts to research and development, recruiting management and technical staff, and raising capital, and has financed its operations through the issuance of ordinary and convertible preferred shares, debt raised under a financing arrangement with Silicon Valley Bank (SVB) including the Paycheck Protection Program loan (PPP loan), a sub-award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) program and the proceeds of a private placement (Private Placement) and subsequent rights offering (the 2020 Rights Offering) pursuant to which its wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda) issued and sold approximately $51.8 million aggregate principal amount of 6.500% Exchangeable Senior Subordinated Notes due 2025 (Exchangeable Notes) and $0.1 million aggregate principal amount of Limited Recourse Royalty-Linked Subordinated Notes (the RLNs and, together with the Exchangeable Notes, the Securities), which Securities were sold in units consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs (the Units). The Company has not generated any product revenue. The Company is subject to risks and uncertainties common to early-stage companies in the pharmaceutical industry, including, but not limited to, the ability to secure additional capital to fund operations, failure to successfully develop and commercialize its product candidates, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology and compliance with government regulations.

Even with receipt of U.S. Food and Drug Administration (FDA) approval, 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.

The Company filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on October 17, 2022 (File No. 333-267795), and pursuant to which the Company registered for sale up to $100.0 million of any combination of debt securities, ordinary shares, preferred shares, subscription rights, purchase contracts, units and/or warrants from time to time and at prices and on terms that the Company may determine. On October 7, 2022, the Company entered into a sales agreement with HC Wainwright (the Sales Agreement), as agent, pursuant to which it could offer and sell ordinary shares, nominal value $0.01 per share (the ordinary shares) for aggregate gross sales proceeds of up to $16.0 million (subject to the availability of ordinary shares), from time to time through HC Wainwright by any method permitted that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended (the Securities Act). On December 10, 2024 the Company filed a prospectus supplement with the Securities and Exchange Commission (SEC) pursuant to which it may offer and sell ordinary shares having an aggregate offering price of up to an additional $25.0 million through HC Wainwright pursuant to the Sales Agreement.

On August 9, 2024, the Company completed a rights offering (the 2024 Rights Offering) in which it sold an aggregate of 6,121,965 units (2024 Units) at a subscription price of $1.21 per whole 2024 Unit, consisting of (a) one ordinary share, (b) a warrant to purchase 0.50 ordinary shares, at an exercise price of $1.21 per whole ordinary share from the date of issuance through its expiration one year from the date of issuance (the 1-year warrants) and (c) a warrant to purchase one ordinary share, at an exercise price of $1.21 per whole ordinary share from the date of issuance through its expiration five years from the date of issuance (the 5-year warrants and, together with the 1-year warrants, the warrants). The Company's net proceeds from the 2024 Rights Offering, after deducting dealer-manager fees and other offering expenses payable by the Company, were $5.4 million. The warrants are exercisable upon issuance at a price of $1.21 per ordinary share. The 1-year warrants expire on August 9, 2025 and the 5-year warrants expire on August 9, 2029.

In accordance with Accounting Standards Update (ASU) 2014-15, *Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events, considered in

aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year of the date of issue of the consolidated financial statements.

The Company has funded its operations to date primarily with proceeds from the sale of preferred shares and ordinary shares, warrants, debt raised under its financing arrangement with SVB including the PPP loan (both of which have been repaid), payments received under the CARB-X program and proceeds of the Private Placement and Rights Offering. The Company has incurred operating losses since inception, including net losses of $24,774, $38,371 and $44,434 for the years ended December 31, 2024, 2023 and 2022, respectively. The Company had an accumulated deficit of $486,072 as of December 31, 2024 and expects to continue to incur net losses for the foreseeable future. The Company's future cash flows are dependent on sales and key variables such as its ability to secure additional sources of funding in the form of public or private financing of debt or equity or collaboration agreements. Based on its available cash and cash equivalents, the Company does not have cash on hand to fund its current operations and capital expenditure requirements for the next 12 months from the date of this Annual Report on Form 10-K. This condition raises substantial doubt about the Company's ability to continue as a going concern for one year from the date these consolidated financial statements are issued.

The Company plans to address this condition by raising funding through the possible sale of the Company's equity or debt through public or private equity financings, which may include sales of the Company's ordinary shares under the Company's Sales Agreement with HC Wainwright. Although management intends to pursue plans to obtain additional funding to finance its operations, and the Company has successfully raised capital in the past, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all. In addition, in parallel, the Company is evaluating its corporate, strategic, financial and financing alternatives, with the goal of maximizing value for its shareholders. These alternatives could potentially include the licensing, sale or divestiture of the Company's assets or proprietary technologies or another strategic transaction involving the Company. The evaluation of corporate, strategic, financial and financing alternatives may not result in any particular action or any transaction being pursued, entered into or consummated, and there is no assurance as to the timing, sequence or outcome of any action or transaction or series of actions or transactions.

If the Company is unable to obtain funding, it could be forced to significantly delay, scale back or discontinue the development and commercialization of its sulopenem program, or otherwise change its strategy, which could adversely affect its business prospects, or the Company may be unable to continue operations. Based on the Company's operating losses since inception, the expectation of continued operating losses for the foreseeable future, and the need to raise additional capital to finance its future operations, management has concluded there is substantial doubt about the Company's ability to continue as a going concern within one year from the date these consolidated financial statements are issued.

The accompanying consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

(2)Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements, the reported amounts of expenses during the reporting period and the assessment of the Company's ability to continue as a going concern. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the valuation of the RLNs. 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.

Specifically, management has estimated variables used to calculate the DCF analysis to value the RLN liability (see Note 3 – Fair Value of Financial Assets and Liabilities).

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 years ended December 31, 2024, 2023 and 2022, respectively, these changes related to unrealized gains and losses on the Company's available-for-sale short-term investments. There were no reclassifications out of comprehensive loss for the years ended December 31, 2024, 2023 and 2022, respectively.

Consolidation

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

Short-term Investments

The Company's investments consisted primarily of debt securities, including investment-grade corporate bonds. The Company considers its portfolio of investments to be available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Investments with maturities beyond one year are generally classified as short term, based on their highly liquid nature and because such marketable securities represent the investment of cash that is available for current operations. Unrealized gains and losses are reported as a component of accumulated other comprehensive loss in shareholders' equity. Realized gains and losses and declines in value are included as a component of interest expense, net based on the specific identification method. Any credit impairments are recorded through an allowance account.

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 Federal Deposit Insurance Corporation (FDIC) up to $250, while accounts held at Irish financial institutions are insured under the Deposit Guarantee Scheme up to $104 (€100).

Cash accounts with any type of restriction are classified as restricted cash. If restrictions are expected to be lifted in the next twelve months, the restricted cash account is classified as current. Included within restricted cash on the Company's consolidated balance sheet is $17 and $17 for the years ended December 31, 2024 and 2023, respectively, relating to the warrants issued on June 5, 2020 pursuant to the securities purchase agreement (June 3, 2020 SPA) in the June 3, 2020 registered direct offering (June 3, 2020 Offering), $6 and $6 for the years ended December 31, 2024 and 2023, respectively, relating to the warrants issued on July 2, 2020 pursuant to the securities purchase agreement (June 30, 2020 SPA) in the June 30, 2020 registered direct offering (June 30, 2020 Offering) and $11 and $11 for the years ended December 31, 2024 and 2023, respectively, relating to warrants issued in the underwritten offering in October 2020 (October 2020 Offering). On the closing date of each of the registered direct offerings in June 2020 (June 3 Offering) and July 2020 (June 30 Offering) and the underwritten offering in the October 2020 Offering, each investor deposited $0.01 per warrant issued being the nominal value of the underlying ordinary share represented by each warrant. This amount will be held in trust by the Company pending a decision by the relevant investor to exercise the warrant by means of a "cashless exercise" pursuant to the terms of the warrant, in which case the $0.01 will be used to pay up the nominal value of the ordinary share issued pursuant to the warrant. Upon the exercise of the warrants other than by means of a "cashless exercise", the amount held in trust will be returned to the relevant investor in accordance with the terms of the applicable purchase agreement or prospectus.

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.

Intangible Assets

The Company's finite-lived intangible assets consist of the regulatory milestone payment payable to Pfizer upon approval of ORLYNVAH™ by the FDA and is stated at cost less accumulated amortization. The Company calculates amortization expense, which is recognized in cost of sales, using the straight-line method over the estimated useful life of the related asset which the Company believes reasonably represents the time period in which the economic benefit of the intangible asset is consumed or otherwise realized. The Company evaluates recoverability of the intangible asset periodically by considering events or changes in circumstances that may warrant revised estimates of useful lives or that indicate the asset may be impaired and, when there were indications that this asset is more likely than not to have become impaired, would test for impairment.

Property and Equipment

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

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

Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in loss from operations. Repairs and maintenance costs are expensed as incurred. The Company reviews the recoverability of all long-lived assets, including the related useful life, whenever events or changes in circumstances indicate that the carrying amount of a long-lived asset might not be recoverable.

Leases

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

Research and Development Expenses

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

Accrued Research and Development Expenses

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

•Vendors, including central laboratories, in connection with preclinical development activities;

•Clinical Research Organizations (CROs), and investigative sites in connection with preclinical studies and clinical trials; and

•Contract Manufacturing Organizations(CMOs), in connection with drug substance and drug product formulation of preclinical and clinical trial materials.

The Company bases expenses related to preclinical studies and clinical trials on estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage preclinical studies and clinical trials on its behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and

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

Patent Costs

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

Share-Based Compensation

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

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 re-measured 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 the consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

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

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

Research and Development Credits

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

Fair Value of Financial Instruments

The 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.

•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 RLNs 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 cash and cash equivalents, prepaid expenses and other current assets, accounts payable, accrued expenses and other liabilities approximate their fair value based on the short-term maturity of these instruments.

Borrowings

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

Derivative Liability

The Company accounted for derivative instruments in accordance with ASC 815, *Derivatives and Hedging*, which establishes accounting and reporting standards for derivative instruments, including certain derivative instruments embedded in other financial instruments or contracts which require bifurcation and measurement at fair value for accounting purposes on the balance sheet date. Any liabilities recorded at fair value were revalued each reporting period with the resulting change in fair value reflected in adjustments to fair value of derivatives.

Royalty-Linked Notes

On recognition, the RLNs qualified as debt instruments under ASC 470, *Debt*, and were initially recorded at fair value, applying a DCF model, and then subsequently measured at amortized cost. In January 2021, the RLNs were exchange listed, and therefore, derivative accounting has been applied in accordance with ASC 815, *Derivatives and Hedging,* which establishes accounting and reporting standards for derivative instruments, including certain derivative instruments embedded in other financial instruments or contracts which require bifurcation and measurement at fair value for accounting purposes on the balance sheet date. Any liabilities recorded at fair value are revalued at each reporting period with the resulting change in fair value reflected in adjustments to fair value of derivatives.

Ordinary Share Warrants

The Company accounts for ordinary share warrants in accordance with applicable accounting guidance provided in ASC 815, *Derivatives and Hedging – Contracts in Entity's Own Equity*, as either derivative liabilities or as equity instruments depending on the specific terms of the warrant agreement. Any warrants that (i) require physical settlement or net-share settlement or (ii) provide the Company with a choice of net-cash settlement or settlement in its own shares (physical settlement or net-share settlement), provided that such warrants are indexed to the Company's own shares is classified as equity. The Company completed a number of offerings containing freestanding derivatives which satisfy the criteria for classification as equity instruments as the warrants do not contain cash settlement features or variable settlement provisions that cause them to not be indexed to the Company's own stock. The Company assesses classification of its ordinary share warrants at each reporting date to determine whether the instruments still qualify for the scope exception under ASC 815, *Derivatives and Hedging*.

Concentration of Credit Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company has most of its cash and cash equivalents at three accredited financial institutions in the United States and Ireland, 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 has a greater than 50% likelihood of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. The Company records interest related to unrecognized tax benefits in interest expense and penalties in general and administrative expenses.

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 following ordinary shares underlying the options, unvested restricted share units, warrants and the Exchangeable Notes have been excluded from the calculation because they would be anti-dilutive.

	Year ended December 31,		
	2024	**2023**	**2022**
Options to purchase ordinary shares	841,720	1,108,988	355,591
Unvested restricted share units	—	16,666	128,728
Warrants	8,164,980	480,178	480,178
Exchangeable Notes	2,815,536	1,255,451	1,287,660
Total	11,822,236	2,861,283	2,252,157

Segment and Other Information

The Company determines and presents operating segments based on the information that is internally provided to the Chief Executive Officer and Chief Financial Officer, who together are considered the Company's chief operating decision maker, in accordance with ASC 280, *Segment Reporting*. The Company has determined that it operates as a single business segment, which is the development and commercialization of innovative treatments for drug resistant bacterial infections. Refer to Note 12 – Segment Reporting for further information related to our segment.

Retirement Plan

The Company has a defined contribution plan under Section 401(k) of the Internal Revenue Code (the 401(k) Plan). The 401(k) Plan covers all U.S. employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pre-tax basis. If the 401(k) Plan is considered top-heavy at the end of the financial year, with key employee accounts accounting for greater than 60% of total 401(k) Plan assets, the Company is required to contribute a deferral rate of up to 3% to the 401(k) Plan on behalf of certain employees. The Company was required to make a top-heavy contribution for the years ended December 31, 2024, 2023 and 2022 of $0.01 million, $0.03 million and $0.02 million, respectively.

Inventory

Inventories are valued at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method for all inventories. The Company's policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. The estimate of excess quantities is subjective and primarily dependent on the estimates of future demand for a particular product. If the estimate of future demand changes, the Company considers the impact on the reserve for excess inventory and adjusts the reserve as required. Increases in the reserve are recorded as charges in cost of product sales. For product candidates that have not been approved by the FDA, inventory used in clinical trials is expensed at the time of production and recorded as research and development expenses. For products that have been

approved by the FDA, inventory used in clinical trials is expensed at the time the inventory is packaged for the clinical trial. Prior to an advisory committee providing a recommendation to the FDA that the Company's application should be approved, costs related to manufacturing the product candidates are recorded as research and development expenses. All direct manufacturing costs incurred after this recommendation will be capitalized into inventory. The Company had no inventory as of December 31, 2024 or December 31, 2023.

Contingent Consideration

Certain license agreements contain milestone payments that could result in the requirement to make contingent consideration payments, see Note 16 – Commitments and Contingencies 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. The Company did not record any contingent consideration amounts as at December 31, 2024 or December 31, 2023.

Recently Adopted Accounting Pronouncements

On November 27, 2023, the FASB issued Accounting Standards Update (ASU) No. 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures (ASU 2023-07), which enhances segment disclosures and requires additional disclosures of segment expenses. This ASU is effective for annual periods in fiscal years beginning after December 15, 2023, and interim periods beginning after December 15, 2024. We adopted this ASU for the annual period ended December 31, 2024 and the amendments have be applied retrospectively to all prior periods presented in the financial statements by expanding the disclosure of expenses included in our segment measures of profitability. Refer to our segments disclosure in Note 12 – Segment Reporting for more information.

Recent Accounting Pronouncements

On October 9, 2023, the FASB issued ASU No. 2023-06, *Disclosure Improvements: Codification Amendments in Response to the SEC's Disclosure Update and Simplification Initiative* (ASU 2023-06), which incorporates into the Codification several disclosures and presentation requirements currently residing in SEC Regulations S-X and S-K. For entities subject to the existing SEC disclosure requirements, including those preparing for sale or issuance of securities, the effective date for each amendment will be the date on which the SEC's removal of that related disclosure from Regulation S-X or Regulation S-K becomes effective, with early adoption prohibited. For all other entities, the amendments will be effective two years later, with early adoption permitted. ASU 2023-06 is not expected to have a material impact on the consolidated financial statements.

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* (ASU 2023-09), which enhances the annual income tax disclosures for the effective tax rate reconciliation and income taxes paid. The amendments are effective for public business entities, for annual periods beginning after December 15, 2024 and for annual periods beginning after December 15, 2025 for all other entities. Early adoption is permitted for annual financial statements that have not yet been issued or made available for issuance. ASU 2023-09 applies on a prospective basis to annual financial statements for periods beginning after the effective date. However, retrospective application in all prior periods presented is permitted. The Company is assessing what impact ASU 2023-09 will have on the consolidated financial statements.

On November 04, 2024, the FASB issued ASU 2024-03, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses* (ASU 2024-03), which requires new disclosures to disaggregate prescribed natural expenses underlying any income statement caption. ASU 2024-03 is effective for annual periods in fiscal years beginning after December 15, 2026, and interim periods thereafter. Early adoption is permitted. ASU 2024-03 applies on a prospective basis for periods beginning after the effective date. However, retrospective application to any or all prior periods presented is permitted. We are currently assessing the impact ASU 2024-03 will have on the consolidated financial statements and disclosures.

On November 26, 2024, the FASB issued ASU 2024-04, *Debt—Debt with Conversion and Other Options (Subtopic 470-20): Induced Conversions of Convertible Debt Instruments* (ASU 2024-04), which clarifies the requirements for determining whether certain settlements of convertible debt instruments should be accounted for as an induced conversion. ASU 2024-04 is effective for all entities for annual and interim periods in fiscal years beginning after December 15, 2025. Early adoption is permitted for all entities that have adopted the amendments in ASU 2020-06. ASU 2024-04 is not expected to have a material impact on the consolidated financial statements.

(3)Fair Value of Financial Assets and Liabilities

The Company did not hold financial assets carried at fair value as of December 31, 2024.

The following table presents information about the Company's financial assets that were carried at fair value on a recurring basis on the consolidated balance sheet as of December 31, 2023 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value.

December 31, 2023				
Assets	**Total**	**Level 1**	**Level 2**	**Level 3**
Short-term investments:				
Corporate bonds	$ 1,179	$ —	$ 1,179	$ —
Commercial paper	3,287	—	3,287	—
U.S. Treasury bonds	13,393	—	13,393	—
	$ 17,859	$ —	$ 17,859	$ —

See Note 4 – Short-term Investments, for details on the short-term investments. The carrying amounts reported in the consolidated balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable, accrued expenses and other current liabilities approximate their fair value based on the short-term maturity of these instruments.

The following table presents information about the Company's Exchangeable Notes, Promissory Note and RLNs and indicates the fair value hierarchy of the valuation inputs utilized to determine the approximate fair value:

December 31, 2024					
Current liabilities	**Book Value**	**Approximate Fair Value**	**Level 1**	**Level 2**	**Level 3**
Exchangeable Notes					
Short-term exchangeable notes	$ 14,463	$ 14,444	$ —	$ 14,444	$ —
Total current liabilities	$ 14,463	$ 14,444	$ —	$ 14,444	$ —
Long-term liabilities					
Promissory Note					
Long-term promissory note	20,300	20,412	—	20,412	—
Revenue Futures					
Royalty-linked notes	10,771	10,771	—	—	10,771
Total	$ 31,071	$ 31,183	$ —	$ 20,412	$ 10,771

December 31, 2023					
Long-term liabilities	**Book Value**	**Approximate Fair Value**	**Level 1**	**Level 2**	**Level 3**
Exchangeable Notes					
Long-term exchangeable notes	$ 11,453	$ 11,645	$ —	$ 11,645	$ —
Revenue Futures					
Royalty-linked notes	7,503	7,503	—	—	7,503
Total	$ 18,956	$ 19,148	$ —	$ 11,645	$ 7,503

The fair value of Exchangeable Notes was determined using DCF analysis using the fixed interest rate outlined in the indenture governing the Exchangeable Notes (Exchangeable Notes Indenture), without consideration of transaction costs, which represents a Level 2 basis of fair value measurement.

The fair value of the long-term Promissory Note was determined using DCF analysis using the fixed interest rate outlined in the license agreement with Pfizer for the worldwide exclusive rights to research, develop, manufacture and commercialize sulopenem (Pfizer License), which represents a Level 2 basis of fair value measurement (see Note 10 – Debt).

The Level 3 liabilities held as of December 31, 2024 and 2023, consist of a separate financial instrument, that was issued as part of the Units, the RLNs (see Note 11 – Royalty-Linked Notes).

At any time on or after January 21, 2021, subject to specified limitations, the Exchangeable Notes are exchangeable for the Company's ordinary shares, cash or a combination of ordinary shares and cash, at an exchange rate of 191.7028 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an exchange price of approximately 5.2164 per ordinary share) as of

December 31, 2024, which was adjusted from an initial exchange rate of 66.666 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of $15.00 per ordinary share) and is subject to further adjustment pursuant to the terms of the Exchangeable Notes Indenture. Beginning on January 21, 2021 to December 31, 2024, certain noteholders of $40,691 aggregate principal amount of Exchangeable Notes have exchanged their notes for an aggregate of 3,760,155 of the Company's ordinary shares, which included accrued and unpaid interest relating to such notes. The aggregate principal amount of Exchangeable Notes outstanding as of December 31, 2024 was $11,117. See Note 18 ─ Subsequent Events for details of repayment of the Exchangeable Notes in January 2025.

The RLN liability is carried at fair value on the consolidated balance sheet (see Note 11 – Royalty-Linked Notes). The total fair value of $10,771 was determined using DCF analysis, without consideration of transaction costs, which represents a Level 3 basis of fair value measurement. The key inputs to valuing the RLNs were the terms of the indenture governing the RLNs (RLN Indenture), the expected cash flows to be received by holders of the RLNs based on management's revenue forecasts of U.S. sulopenem sales and a discount rate to derive the net present value of expected cash flows. The RLNs will be subject to a maximum return amount, including all principal and payments and certain default interest in respect of uncurable defaults, of $160.00 (or 4,000 times the principal amount of such note). The discount rate applied to the model was 22% for the years ended December 31, 2024 and 2023. Fair value measurements are highly sensitive to changes in these inputs and significant changes in these inputs could result in a significantly higher or lower fair value.

There have been no transfers of assets or liabilities between the fair value measurement levels.

(4)Short-term Investments

The Company classifies its short-term investments as available-for-sale. Short-term investments comprise highly liquid investments with minimum "A-" rated securities and have maturities of more than three months at the date of purchase. 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 amortized cost and fair value of investments are represented by unrealized gains or losses. The fair value of U.S. Treasury bonds, corporate bonds and commercial paper are represented by Level 2 fair value measurements - quoted price for a similar asset, or other observable inputs such as interest rates or yield curves.

The Company did not hold any short-term investments for the year ended December 31, 2024.

The following table represents the Company's available for sale short-term investments by major security type as of December 31, 2023:

December 31, 2023					Maturity by period	
Available-for-sale	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Fair Value Total	Less than 1 Year	1 to 5 Years
Corporate bonds	$ 1,179	$ 1	$ —	$ 1,180	$ 1,180	$ —
Commercial paper	3,288	—	(1)	3,287	3,287	—
U.S. Treasury bonds	13,391	3	(2)	13,392	13,392	—
Total	$ 17,858	$ 4	$ (3)	$ 17,859	$ 17,859	$ —

(5)Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following:

	December 31, 2024	December 31, 2023
Prepaid insurance	$ 389	$ 472
Other prepaid assets	138	89
Right of use assets, net	65	—
Research and development tax credit receivable	18	195
Prepaid research and development expenses	4	872
Total	$ 614	$ 1,628

(6)Intangible Asset, net

Intangible asset and related accumulated amortization are as follows:

	December 31, 2024	December 31, 2023
Gross intangible asset	$ 20,000	$ —
Less: accumulated amortization	(254)	—
	$ 19,746	$ —

On November 18, 2015, the Company and Iterum Therapeutics International Limited (ITIL), a wholly owned subsidiary of the Company, entered into the Pfizer License. Under the Pfizer License, ITIL agreed to make certain regulatory and sales payments, including a regulatory milestone payment of $20.0 million to Pfizer upon approval of ORLYNVAH™ by the FDA for commercial sale in the United States. On October 25, 2024, the Company received FDA approval for ORLYNVAH™ (sulopenem etzadroxil and probenecid) for the treatment of uncomplicated urinary tract infections in adult women who have limited or no alternative oral antibacterial treatment options, and the regulatory milestone payment was capitalized on that date. The milestone payment is being amortized over a period of 14.4 years based on the patent life of ORLYNVAH™ and the amortization is recorded as cost of sales. The Company deferred this payment for a two-year period, at an annual rate of eight percent on a daily compounded basis until paid in full, as was permitted pursuant to the terms of the Pfizer License.

The estimated future amortization related to intangible assets included on the consolidated balance sheet as of December 31, 2024 for the following five fiscal years and thereafter were as follows:

Due in 12 month period ended December 31,	
2025	$ 1,389
2026	1,389
2027	1,389
2028	1,389
2029	1,389
Thereafter	12,801
	$ 19,746

The preceding expected amortization expense is an estimate. Actual amounts of amortization expense may differ from estimated amounts due to additional intangible asset acquisitions, measurement period adjustments to intangible assets, impairments of intangible assets, accelerated amortization of intangible assets, and other events.

(7)Property and Equipment, net

Property and equipment and related accumulated depreciation are as follows:

	December 31, 2024	December 31, 2023
Leasehold improvements	$ 148	$ 148
Furniture and fixtures	120	120
Computer equipment	95	98
	363	366
Less: accumulated depreciation	(340)	(315)
	$ 23	$ 51

Depreciation expense was $30, $31 and $84 for the years ended December 31, 2024, 2023 and 2022, respectively. In addition, accumulated depreciation decreased by $5 due to the removal of fully depreciated computer equipment during the year ended December 31, 2024.

(8)Leases

The Company has entered into a number of operating leases, primarily for office space and commercial property. These leases have remaining terms which range from 0.08 years to 0.58 years. The renewal option on one lease was exercised in February 2022 for an additional period of three years, extending this lease term to June 2025. A Deed of Assignment was signed in August 2023 in relation to a commercial property lease and accordingly the related Right of Use asset and lease liability were derecognized. In

September 2020, the Company entered into a sublease agreement for a commercial unit. This sublease agreement was assigned with the related lease in August 2023.

In November 2021, the Company entered into a 12-month lease, with a rolling extension, for office space, and in May 2022, the Company entered into a 6-month lease for office space, which was extended to November 2023, and elected not to apply the measurement and recognition requirements of ASC 842 to these short-term leases as any renewal term exercised or considered reasonably certain of exercise by the Company did not extend more than 12 months from the end of the previously determined lease term. In August 2023, the Company extended the lease agreements for a further nine months, with a rolling extension, and twelve months, respectively. While neither of the extended agreements were for more than 12 months from the end of the previously determined lease term, it was considered to be reasonably certain that these lease arrangements would be extended beyond a period of more than 12 months. Accordingly, the Company applied the measurement and recognition requirements of ASC 842 to these lease arrangements. In September 2024, the Company notified the landlord of its intention to terminate the twelve month lease on November 30, 2024 and in October 2024, the Company notified the landlord of its intention to terminate the lease with the rolling extension on January 31, 2025 and the related Right of Use assets and lease liabilities have accordingly been reduced.

Certain leases contain variable lease payments, including payments based on an index or rate. Variable lease payments based on an index or rate are initially measured using the index or rate in effect at lease commencement. Certain agreements contain both lease and non-lease components. The Company has elected to separately account for these components in determining the lease liabilities and right-of-use assets. The Company's lease agreements generally do not provide an implicit borrowing rate; therefore, an internal incremental borrowing rate was determined based on information available at lease commencement date for the purposes of determining the present value of lease payments. The Company used the incremental borrowing rate on January 1, 2019 for all leases that commenced prior to that date.

All operating lease expenses are recognized on a straight-line basis over the lease term. The Company recognized $389, $363 and $753 of operating lease costs for right-of-use assets during the years ended December 31, 2024, 2023 and 2022, respectively. The Company recognized $5, $194 and $243 of rental expenses on short-term leases during the .years ended December 31, 2024, 2023 and 2022, respectively. The Company did not recognize any sublease income during the year ended December 31, 2024. The Company recognized $199 and $293 of sublease income during the years ended December 31, 2023 and 2022, respectively.

Information related to the Company's right-of-use assets and related lease liabilities is as follows:

	December 31, 2024	December 31, 2023
Cash paid for operating lease liabilities	$ 385	$ 354

	December 31, 2024	December 31, 2023
Weighted-average remaining lease term	0.39 years	1.46 years
Weighted-average discount rate	11.5 %	12.9 %

Right-of-use assets and lease liabilities for the Company's operating leases were recorded in the consolidated balance sheet as follows, representing the Company's right to use the underlying asset for the lease term ("Prepaid expenses and other current assets" and "Other assets") and the Company's obligation to make lease payments ("Other current liabilities" and "Other liabilities"):

	December 31, 2024	December 31, 2023
Prepaid expenses and other current assets	$ 65	$ —
Other assets	—	549
Total lease assets	65	549
Other current liabilities	$ 67	$ 365
Other liabilities	—	188
Total lease liabilities	$ 67	$ 553

Future lease payments included in the measurement of lease liabilities on the consolidated balance sheet as of December 31, 2024 for the following five fiscal years and thereafter were as follows:

Due in 12 month period ended December 31,		
2025	$	68
2026		—
2027		—
2028		—
2029		—
Thereafter		—
	$	68
Less imputed interest		(1)
Total lease liabilities	$	67

(9)Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2024	December 31, 2023
Accrued manufacturing expenses	$ 1,148	$ 71
Accrued payroll and bonus expenses	1,138	2,742
Accrued professional fees	246	37
Accrued other expenses	74	76
Accrued clinical trial costs	45	4,835
Total	$ 2,651	$ 7,761

(10)Debt

Secured Credit Facility

On April 27, 2018, the Company's subsidiaries, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited (the Borrowers), entered into a loan and security agreement (the Loan and Security Agreement) with SVB pursuant to which SVB agreed to lend the Borrowers up to $30,000 in two term loans. $15,000 of the secured credit facility was funded on closing. A second draw of up to $15,000 was available to the Company through October 31, 2019, upon satisfaction of either of the following: (i) the achievement by the Company of both non-inferiority and superiority primary endpoints from its Phase 3 uncomplicated urinary tract infection (uUTI) trial, as well as reporting satisfactory safety data from the trial, or (ii) the achievement of non-inferiority primary endpoints from both its Phase 3 uUTI and complicated urinary tract infection (cUTI) trials, as well as reporting satisfactory safety data from the trials. The Company did not satisfy the conditions for the second draw before the deadline of October 31, 2019.

Required monthly amortization payments for the initial $15,000 draw commenced on November 1, 2019 and total principal repayments of $1,552 were made during the year ended December 31, 2022. Interest accrued 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 was payable monthly in arrears. All outstanding principal, plus a 4.20% final interest payment, were due and paid on March 1, 2022 (the maturity date), effectively terminating the Loan and Security Agreement. The final payment fee of $630, which represented 4.2% of the funded loan, was accreted using the effective interest method over the life of the loan as interest expense.

In connection with the initial $15,000 draw, the Company issued SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B convertible preferred shares (which converted into warrants to purchase 1,326 ordinary shares upon the Company's initial public offering (IPO)) at an exercise price of $282.75 per share. These warrants will expire on April 27, 2028.

The loan proceeds were allocated based on the relative fair values of the debt instrument and the warrant instrument. The fair value of the warrants and the closing costs were recorded as debt discounts and are being amortized using the effective interest rate method over the term of the loan. The effective annual interest rate of the outstanding debt was approximately 12.51% on March 1, 2022. The Company recognized $16 of interest expense related to the Loan and Security Agreement during the year ended December 31, 2022 including $6 related to the accretion of the debt discounts and deferred financing costs during the year ended

December 31, 2022. All outstanding amounts were repaid on March 1, 2022, effectively terminating the Loan and Security Agreement.

In connection with the Private Placement, Iterum Bermuda was joined as a party to the Loan and Security Agreement as a borrower and the Loan and Security Agreement was amended on January 16, 2020 to, among other things, modify the definition of subordinated debt to include the RLNs and Exchangeable Notes.

2025 Exchangeable Notes

On January 21, 2020, the Company completed a Private Placement pursuant to which its wholly owned subsidiary, Iterum Bermuda issued and sold $51,588 aggregate principal amount of Exchangeable Notes and $103 aggregate principal amount of RLNs, to a group of accredited investors. On September 8, 2020, the Company completed a Rights Offering pursuant to which Iterum Bermuda issued and sold $220 aggregate principal amount of Exchangeable Notes and $0.5 aggregate principal amount of RLNs, to existing shareholders. The Securities were sold in Units with each Unit consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs. The Units were sold at a price of $1,000 per Unit.

At any time on or after January 21, 2021, subject to specified limitations, the Exchangeable Notes are exchangeable for the Company's ordinary shares, cash or a combination of ordinary shares and cash, at the Company's election, at an exchange rate of 191.7028 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an exchange price of approximately 5.2164 per ordinary share) as of December 31, 2024, which exchange rate was adjusted from an initial exchange rate of 66.666 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of $15.00 per ordinary share) and is subject to further adjustment pursuant to the terms of the Exchangeable Notes Indenture. Any accrued and unpaid interest being exchanged will be calculated to include all interest accrued on the Exchangeable Notes being exchanged to, but excluding, the exchange settlement date. Beginning on January 21, 2021 to December 31, 2024, certain noteholders of $40,691 aggregate principal amount of Exchangeable Notes have completed a non-cash exchange of their notes for an aggregate of 3,760,155 of the Company's ordinary shares, which included accrued and unpaid interest relating to such notes. The aggregate principal amount of Exchangeable Notes outstanding as of December 31, 2024 was $11,117. See Note 18 – Subsequent Events for details of repayment of the Exchangeable Notes in January 2025.

In addition, the Exchangeable Notes will become due and payable by the Company upon the occurrence of a Fundamental Change as defined in the Exchangeable Notes Indenture. The Company will be required to pay each holder of the Exchangeable Notes the greater of three times the outstanding principal amount of such Exchangeable Note and the consideration that would be received by the holder of such Exchangeable Note in connection with such Fundamental Change if the holder had exchanged its note for ordinary shares immediately prior to the consummation of such Fundamental Change, plus any accrued and unpaid interest.

The Company evaluates its debt and equity issuances to determine if those contracts, or embedded components of those contracts, qualify as derivatives under ASC 815-15, *Derivatives and Hedging*, requiring separate recognition in the Company's financial statements. The Company evaluated the accounting for the issuance of the Exchangeable Notes and concluded that the embedded exchange option and change of control feature are considered a derivative liability under ASC 815-15 requiring bifurcation, from the Exchangeable Notes, as it does not qualify for the scope exceptions for contracts in an entity's own equity given the terms of the Exchangeable Notes. The exchange option and change of control feature are accounted for as a derivative liability, under ASC 815-15, and are required to be separated and recorded as a single liability, which is revalued each reporting period with the resulting change in fair value reflected in other income, net, in the consolidated statements of operations and comprehensive loss.

The fair value of the derivative liability related to the Private Placement on January 21, 2020 was $27,038, and the fair value of the derivative liability related to the Rights Offering on September 8, 2020 was $82, both of which were recorded as a reduction to the book value of the host debt contract. This debt discount is being amortized to interest expense over the term of the debt using the effective interest method. Transaction costs amounting to $2,848 were allocated to the exchange option. These costs are reflected in financing transaction costs in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2020. Transaction costs amounting to $2,814 were allocated to the debt host and capitalized in the host debt book value.

In circumstances where the embedded exchange option in a convertible instrument is required to be bifurcated, and there are other embedded derivative instruments in the convertible instrument that are required to be bifurcated, the derivative instruments are accounted for as a single, compound derivative instrument. The classification of derivative instruments, including whether such instruments should be recorded as liabilities or as equity, is reassessed at the end of each reporting period. Derivative instrument liabilities are classified in the balance sheet as current or non-current based on whether or not settlement of the derivative instrument is expected within twelve months of the balance sheet date.

The Company determined that all other features of the Exchangeable Notes were clearly and closely associated with a debt host and did not require bifurcation as a derivative liability. The initial value of the Exchangeable Notes on inception, net of transaction costs was $9,891.

The Company recognized $723, $811 and $820 of interest expense related to the Exchangeable Notes during the years ended December 31, 2024, 2023 and 2022, respectively, and $2,288, $2,339 and $2,344 related to the amortization of the debt discounts and deferred financing costs during the years ended December 31, 2024, 2023 and 2022, respectively. These amounts are recorded in interest expense, net in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2024, 2023 and 2022, respectively. The balance of the Exchangeable Notes at each reporting date is as follows:

	December 31, 2024	
	Principal	Accrued Interest
January 2020 $1,000 Exchangeable Notes, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	$ 51,588	$ 6,576
September 2020 $1,000 Exchangeable Notes, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	220	36
Conversion of $1,000 Exchangeable Notes, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	(40,691)	(3,071)
2025 Exchangeable Notes	11,117	3,541
Unamortized discount and debt issuance costs	(195)	—
2025 Exchangeable Notes, net	$ 10,922	$ 3,541

	December 31, 2023	
	Principal	Accrued Interest
January 2020 $1,000 Exchangeable Notes, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	$ 51,588	$ 5,861
September 2020 $1,000 Exchangeable Notes, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	220	28
Conversion of $1,000 Exchangeable Notes, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	(40,691)	(3,071)
2025 Exchangeable Notes	11,117	2,818
Unamortized discount and debt issuance costs	(2,482)	—
2025 Exchangeable Notes, net	$ 8,635	$ 2,818

Payment Protection Program

On April 3, 2020, the U.S. Small Business Administration (SBA) launched the Paycheck Protection Program, which was established following the signing of the CARES Act on March 27, 2020. On April 30, 2020, our wholly owned subsidiary, Iterum Therapeutics US Limited (Iterum US Limited), entered into the PPP loan with SVB under the Paycheck Protection Program, pursuant to the Company receiving a PPP loan of $744 with a fixed 1% annual interest rate and a maturity of two years. Under the terms of the agreement, there were no payments due by the Company until the SBA remitted the forgiveness amount to Iterum US Limited or until after the 10 months after the end of the six-month period beginning April 30, 2020 (the Deferral Period). Following the Deferral Period, equal monthly repayments of principal and interest were due to fully amortize the principal amount outstanding on the PPP loan by the maturity date. The SBA forgave $340 of the loan in November 2020, and the remaining loan of $404 began amortization in December 2020 with equal monthly repayments through March 2022. Total principal repayments of $69 were made during the year ended December 31, 2022. The Company recognized $0 of interest expense related to the loan agreement during the year ended December 31, 2022. All outstanding amounts were repaid on March 17, 2022, effectively terminating the PPP loan.

Pfizer Promissory Note

On November 18, 2015, the Company and ITIL entered into the Pfizer License. Under the Pfizer License, ITIL agreed to make certain regulatory and sales milestone payments, including a regulatory milestone payment of $20.0 million to Pfizer upon approval of oral sulopenem for commercial sale in the United States by the FDA. On October 25, 2024, the Company received FDA approval for ORLYNVAH™ (sulopenem etzadroxil and probenecid) for the treatment of uncomplicated urinary tract infections caused by the designated microorganisms *Escherichia coli, Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women who have limited or no alternative oral antibacterial treatment options. On October 28, 2024, the Company notified Pfizer that it was electing to defer payment of the milestone payment for two years, or until October 25, 2026 (the Deferral Period), and delivered a promissory note (the

Promissory Note) issued by ITIL in the amount of the milestone payment to Pfizer, as permitted pursuant to the terms of the Pfizer License.

The Promissory Note bears interest at an annual rate of eight percent (8.0%) on a daily compounded basis until paid in full and matures on October 25, 2026. ITIL has the right to prepay the unpaid principal balance of the Promissory Note together with accrued and unpaid interest at any time without premium or penalty. Pursuant to the terms of the Promissory Note, ITIL may (i) assign the Promissory Note to an affiliate of ITIL; (ii) designate one of its affiliates to perform its obligations thereunder; or (iii) assign the Promissory Note in the event of a change of control, provided that in the case of clauses (i) and (ii) ITIL is not relieved of any liability thereunder. Pursuant to the terms of the Pfizer License, if a change of control of ITIL or the Company occurs during the Deferral Period, Pfizer may, in its sole discretion and at its sole option, declare the milestone payment to be immediately due and payable together with all interest accrued under the Promissory Note. The Company has guaranteed all of the amounts payable by ITIL under the terms of the Pfizer License, including the amounts owed under the Promissory Note, pursuant to the guarantee entered into by and among ITIL, the Company and Pfizer on November 18, 2015 in connection with the Pfizer License.

Principal Payments on Outstanding Debt

Scheduled principal payments on outstanding debt, including principal amounts owed to RLN holders (see Note 11 – Royalty-Linked Notes) as of December 31, 2024, for the following five fiscal years and thereafter were as follows:

Year Ending December 31,		
2025	$	11,117
2026		20,000
2027		—
2028		—
2029		—
Thereafter		104
	$	31,221

(11)Royalty-Linked Notes

Liability Related to Sale of Future Royalties

On January 21, 2020, as part of the Private Placement, the Company issued 2,579,400 RLNs to a group of accredited investors. On September 8, 2020, as part of the Rights Offering, the Company issued 11,000 RLNs to existing shareholders. The RLNs will entitle the holders thereof to payments, at the applicable payment rate, based solely on a percentage of the Company's net revenues from U.S. sales of specified sulopenem products earned through December 31, 2045, but will not entitle the holders thereof to any payments unless the Company receives FDA approval for one or more specified sulopenem products prior to December 31, 2025 and the Company earns net revenues on such product. If any portion of the principal amount of the outstanding RLNs, equal to $0.04 per RLN, has not been paid as of the end date on December 31, 2045, Iterum Bermuda must pay the unpaid portion of the principal amount. The RLNs will earn default interest if the Company breaches certain obligations under the RLN Indenture (but do not otherwise bear interest) and will be subject to a maximum return amount, including all principal and payments and certain default interest in respect of uncurable defaults, of $160 (or 4,000 times the principal amount of such note). The RLNs are redeemable at any time, at the Company's option, subject to the terms of the RLN Indenture.

In accordance with exceptions allowed under ASC 815-10, *Derivatives and Hedging*, this transaction was initially accounted for as a debt liability under ASC 470. Subsequent to the listing of the RLNs on the Bermuda Stock Exchange in January 2021, the RLNs are accounted for as a derivative and are remeasured to fair value at each reporting date. In accordance with ASC 815, the fair value of the RLNs is determined using DCF analysis, without consideration of transaction costs, which represents a Level 3 basis of fair value measurement. Fair value measurements are highly sensitive to changes in inputs and significant changes to inputs can result in a significantly higher or lower fair value. The Company periodically assesses the revenue forecasts of the specified sulopenem products and the related payments. The Company has no obligation to pay any amount to the noteholders until the net revenue of the specified products are earned.

The balance of the RLNs at each reporting date is as follows:

		December 31, 2024
Total liability related to the sale of future royalties, on inception	$	10,990
Liability related to the sale of future royalties, arising from the Rights Offering		51
Amortization of discount and debt issuance costs		3,666
Adjustments to fair value		(3,936)
Total liability related to the sale of future royalties at December 31, 2024	$	10,771
Current Portion		—
Long-term Portion	$	10,771

		December 31, 2023
Total liability related to the sale of future royalties, on inception	$	10,990
Liability related to the sale of future royalties, arising from the Rights Offering		51
Amortization of discount and debt issuance costs		3,666
Adjustments to fair value		(7,204)
Total liability related to the sale of future royalties at December 31, 2023	$	7,503
Current Portion		—
Long-term Portion	$	7,503

(12) Segment Reporting

In accordance with FASB ASC Topic 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 financial results of the Company's operations are managed and reported to the Chief Executive Officer (CEO) and Chief Financial Officer (CFO), who together are considered the Company's chief operating decision maker (CODM), on a consolidated basis. The CODM assesses performance and allocates resources based on the Company's consolidated statements of operations and key components and processes of the Company's operations are managed centrally. Segment asset information is not used by the CODM to allocate resources.

As a single reportable segment entity, the Company's segment performance measure is net income / (loss) attributable to shareholders. Significant segment expenses, as provided to the CODM, are presented below.

		Years Ended December 31,				
		2024		2023		2022
Segment cost of sales (a)	$	—	$	—	$	—
Segment research and development (b) (c) (d)		(10,247)		(37,842)		(14,456)
Segment general and administration (c) (d)		(7,789)		(7,092)		(9,369)
Share-based compensation expense (see Note 14)		(376)		(784)		(4,758)
Depreciation and amortization		(284)		(1,750)		(1,800)
Operating loss	$	(18,696)	$	(47,468)	$	(30,383)

a)Amortization expense of $254 related to the Pfizer Intangible asset has been excluded for the year ended December 31, 2024 and included within depreciation and amortization.

b)Amortization expense of $1,719 and $1,716 related to the ACSD intangible asset has been excluded for the years ended December 31, 2023 and 2022, respectively, and included within depreciation and amortization.

c)Share-based payment expense of $193, $412 and $1,396 related to research and development and $170, $372 and $3,362 related to general and administration have been excluded for the years ended December 31, 2024, 2023 and 2022, respectively, and included within share-based compensation expense.

d)Depreciation expense of $18, $19 and $49 related to research and development and $12, $12 and $35 related to general and administration have been excluded for the years ended December 31, 2024, 2023 and 2022, respectively, and included within depreciation and amortization.

Interest Expense, Net

	Years Ended December 31,		
	2024	2023	2022
Interest income	$ 789	$ 1,722	$ 819
Interest expense	(3,311)	(3,150)	(3,180)
Interest expense, net	$ (2,522)	$ (1,428)	$ (2,361)

Long-Lived Assets

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

Long lived assets	December 31, 2024	December 31, 2023
Ireland	$ 19,759	$ 342
U.S.	15	287
Total	$ 19,774	$ 629

(13)Shareholders' Equity / (Deficit)

The Company's capital structure consists of ordinary shares and undesignated preferred shares. Under Irish law, the Company is prohibited from allotting shares without consideration. Accordingly, at least the nominal value of the shares issued underlying any warrant, pre-funded warrant, restricted share award, restricted share unit, performance share award, bonus share or any other share based grant must be paid pursuant to the Irish Companies Act 2014 (Irish Companies Act).

Ordinary Shares

On August 9, 2024, the Company completed the 2024 Rights Offering in which it sold an aggregate of 6,121,965 2024 Units. Aggregate gross proceeds to the Company's from the 2024 Rights Offering were $7.4 million and net proceeds were $5.4 million after deducting fees payable to the dealer-manager fees and other offering expenses payable by the Company.

At the Company's annual general meeting of shareholders on May 3, 2023, the Company's shareholders approved an increase of 60,000,000 ordinary shares of $0.01 par value each to the number of authorized ordinary shares and the Company's Articles of Association were amended accordingly. The Company has authorized ordinary shares of 80,000,000 ordinary shares of $0.01 par value each as of December 31, 2024. The holders of ordinary shares are entitled to one vote for each share held. There are no redemption or sinking fund provisions with respect to the authorized ordinary shares.

The Company filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on October 17, 2022 (File No. 333-267795), and pursuant to which the Company registered for sale up to $100.0 million of any combination of debt securities, ordinary shares, preferred shares, subscription rights, purchase contracts, units and/or warrants from time to time and at prices and on terms that the Company may determine.

On October 7, 2022, we entered into the Sales Agreement with HC Wainwright, as agent, pursuant to which the Company could offer and sell ordinary shares for aggregate gross sales proceeds of up to $16.0 million (subject to the availability of ordinary shares), from time to time through HC Wainwright by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act. On December 10, 2024 the Company filed a prospectus supplement with the Securities and Exchange Commission pursuant to which it may offer and sell ordinary shares having an aggregate offering price of up to an additional $25.0 million through HC Wainwright pursuant to the Sales Agreement. During the years ended December 31, 2024 and 2023, the Company sold 10,327,787 and 639,825 ordinary shares under the Sales Agreement at an average price of $1.94 and $1.68 per share for net proceeds of $19,405 and $1,034 respectively.

On February 3, 2021, the Company entered into an underwriting agreement (the Underwriting Agreement) pursuant to which it issued and sold 2,318,840 ordinary shares, $0.01 nominal value per share, at a public offering price per share of $17.25 (the February 2021 Underwritten Offering). The February 2021 Underwritten Offering closed on February 8, 2021. Pursuant to the Underwriting Agreement, the Company granted the underwriter an option for a period of 30 days to purchase up to an additional 347,826 ordinary shares on the same terms and conditions, which the underwriter exercised in full on February 10, 2021. This exercise increased the total number of ordinary shares sold by the Company in the offering to 2,666,666 shares, which resulted in aggregate gross proceeds of $46,000 and net proceeds of $42,119 after deducting underwriting discounts and commissions and other offering expenses.

On February 9, 2021, the Company completed a registered direct offering (the February 2021 Registered Direct Offering), pursuant to which the Company issued and sold an aggregate of 1,166,666 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $30.00, for aggregate gross proceeds of $35,000 and net proceeds of $32,235 after deducting placement agent fees and other offering expenses. The closing date of the February 2021 Registered Direct Offering was February 12, 2021. The Company offered the ordinary shares in the June 3, 2020 Offering, June 30, 2020 Offering, February 2021 Underwritten Offering and February 2021 Registered Direct Offering pursuant to its universal shelf registration statement on Form S-3, which was declared effective on July 16, 2019 (File No. 333-232569).

Beginning on January 21, 2021 to December 31, 2024, certain noteholders of $40,691 aggregate principal amount of Exchangeable Notes have exchanged their notes for an aggregate of 3,760,155 of the Company's ordinary shares, which included accrued and unpaid interest relating to such notes. The aggregate principal amount of Exchangeable Notes outstanding as of December 31, 2024 was $11,117. See Note 18 – Subsequent Events for details of repayment of the Exchangeable Notes in January 2025.

Warrants to purchase Ordinary Shares

In connection with the initial drawdown under the Loan and Security Agreement, the Company issued SVB and LSF warrants to purchase an aggregate of 19,890 Series B convertible preferred shares (which converted into warrants to purchase 1,326 ordinary shares upon the Company's IPO) at an exercise price of $282.75 per share. These warrants will expire on April 27, 2028. No warrants had been exercised as of December 31, 2024.

In connection with the June 3, 2020 Offering completed on June 5, 2020, pursuant to the June 3, 2020 SPA, in a concurrent private placement, the Company issued and sold to institutional investors warrants to purchase up to 99,057 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $24.30 per ordinary share, subject to adjustment in certain circumstances, and will expire on December 5, 2025. Warrants to purchase 13,868 ordinary shares, amounting to 7% of the ordinary shares issued under the June 3, 2020 SPA, were issued to designees of the placement agent on the closing of the June 3, 2020 Offering. Upon closing, the warrants issued to such designees were exercisable immediately at an exercise price of $31.5465 per ordinary share and will expire on June 3, 2025. No warrants had been exercised as of December 31, 2024.

In connection with the June 30, 2020 Offering completed on July 2, 2020, pursuant to the June 30, 2020 SPA, in a concurrent private placement, the Company has also issued and sold to institutional investors warrants to purchase up to 112,422 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $21.30 per ordinary share, subject to adjustment in certain circumstances, and will expire on January 2, 2026. Warrants to purchase 15,739 ordinary shares, amounting to 7% of the ordinary shares issued under the June 30, 2020 SPA, were issued to designees of the placement agent on closing of the June 30, 2020 Offering. Upon closing, the warrants issued to such designees were exercisable immediately at an exercise price of $27.7965 per ordinary share and will expire on June 30, 2025. As of December 31, 2024, warrants issued in connection with the June 30, 2020 Offering had been exercised for 84,317 ordinary shares, for net proceeds of $1,796.

In connection with the October 2020 Offering, the Company issued and sold warrants to purchase up to 1,346,153 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $9.75 per ordinary share, subject to adjustment in certain circumstances, and will expire on October 27, 2025. Warrants to purchase 125,641 ordinary shares, which represents a number of ordinary shares equal to 7.0% of the aggregate number of ordinary shares and pre-funded warrants sold in the October 2020 Offering, were issued to designees of the placement agent on closing of the October 2020 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $12.1875 per ordinary share and expire on October 22, 2025. As of December 31, 2024, warrants issued in connection with the October 2020 Offering had been exercised for 1,392,701 ordinary shares, for net proceeds of $13,885.

In connection with the February 2021 Underwritten Offering, the Company issued to the underwriter's designees warrants to purchase 162,318 ordinary shares, amounting to 7.0% of the aggregate number of ordinary shares sold in the February 2021 Underwritten Offering which closed on February 8, 2021. The warrants issued to such designees have an exercise price of $21.5625 per ordinary share, were exercisable upon issuance and will expire on February 3, 2026. As of December 31, 2024, warrants issued in connection with the February 2021 Underwritten Offering had been exercised for 25,333 ordinary shares, for net proceeds of $546.

In connection with the February 2021 Underwritten Offering, the Company granted the underwriter an option for a period of 30 days to purchase an additional 347,826 ordinary shares. Upon the underwriter's exercise of its option, on February 10, 2021, the Company issued warrants to purchase an additional 24,347 ordinary shares to the underwriter's designees, amounting to 7.0% of the aggregate number of additional ordinary shares sold pursuant to the underwriter's option. The warrants issued to such designees have an exercise price of $21.5625 per ordinary share, were exercisable upon issuance and will expire on February 3, 2026. No warrants had been exercised as of December 31, 2024.

In connection with the February 2021 Registered Direct Offering which closed on February 12, 2021, warrants to purchase 81,666 ordinary shares, amounting to 7.0% of the aggregate number of ordinary shares issued under the securities purchase agreement, were issued to designees of the placement agent upon closing. The warrants issued to such designees were exercisable upon issuance at an exercise price of $37.50 per ordinary share and will expire on February 9, 2026. No warrants had been exercised as of December 31, 2024.

In connection with the 2024 Rights Offering, the Company issued and sold 1-year warrants to purchase up to 3,060,982 ordinary shares and 5-year warrants to purchase up to 6,121,965 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $1.21 per ordinary share and will expire on August 9, 2025 and August 9, 2029, respectively. As of December 31, 2024, 1-year warrants issued in connection with the 2024 Rights Offering were exercised for 850,998 ordinary shares for net proceeds of $1,030 and 5-year warrants issued in connection with the 2024 Rights Offering were exercised for 647,147 ordinary shares for net proceeds of $783.

The Company has classified the warrants as equity in accordance with ASC 815. Accordingly, the proceeds were allocated between ordinary shares, the 1-year warrants and the 5-year warrants based on the relative fair value of the individual components. The fair value of the warrants were determined using a Black-Scholes option pricing model and the ordinary shares based on the closing date share price and were recorded in additional paid-in capital within shareholders' deficit on the consolidated balance sheets. The following assumptions were used in the Black-Scholes option pricing model:

	August 9, 2024	
	1-year warrants	5-year warrants
Volatility	109 %	109 %
Expected term in years	1.00	5.00
Dividend rate	0 %	0 %
Risk-free interest rate	4.50 %	3.80 %
Share price	$ 1.18	$ 1.18
Strike price	$ 1.21	$ 1.21
Fair value of warrants issued	$ 0.50	$ 0.94

Undesignated Preferred Shares

The Company has authorized 100,000,000 undesignated preferred shares of $0.01 par value each as of December 31, 2024. The Company's Board of Directors is authorized by the Company's Articles of Association to determine the rights attaching to the undesignated preferred shares including rights of redemption, rights as to dividends, rights on winding up and conversion rights. There were no undesignated preferred shares in issue as of December 31, 2024 or December 31, 2023.

(14)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 14,895 ordinary shares in the form of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units and other share awards. The types of share-based awards, including the rights amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors. The purpose of the 2015 Plan was to provide the Company with the flexibility to issue share-based awards as part of an overall compensation package to attract and retain qualified personnel. On May 18, 2017, the Company amended the 2015 Plan to increase the number of ordinary shares available for issuance under the 2015 Plan by 14,640 shares to 29,535 shares.

On March 14, 2018, the Company's Board of Directors adopted and approved the 2018 Equity Incentive Plan (the 2018 Plan), which became effective upon the execution and delivery of the underwriting agreement related to the Company's IPO in May 2018. Since adopting the 2018 Plan, no further grants will be made under the 2015 Plan. The ordinary shares underlying any options that are forfeited, canceled, repurchased or are otherwise terminated by the Company under the 2015 Plan will not be added back to the ordinary shares available for issuance.

The 2018 Plan originally authorized the Company to grant up to 67,897 ordinary shares in the form of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units, performance share awards, performance cash awards and other share awards. The types of share-based awards, including the amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors. The ordinary shares underlying any options that are forfeited, canceled, repurchased or are otherwise terminated by the Company under the 2018 Plan are added back to the ordinary shares available for issuance under the 2018 Plan.

On December 5, 2018, pursuant to powers delegated to it by the Board of Directors of the Company, the Compensation Committee approved an increase in the number of ordinary shares available to be granted pursuant to the 2018 Plan by 4% of the total number of shares of the Company's issued share capital on December 31, 2018, being 38,272 ordinary shares.

On February 14, 2020, pursuant to powers delegated to it by the Board of Directors of the Company, the Compensation Committee approved, by written resolution, an increase of 39,650 ordinary shares to the number of ordinary shares available to be granted pursuant to the 2018 Plan, being just under 4% of the total number of the Company's ordinary shares outstanding on December 31, 2019, in accordance with the terms of the 2018 Plan.

On June 10, 2020, at the Company's annual general meeting of shareholders, the shareholders approved and adopted an Amended and Restated 2018 Plan which, among other things included an increase of 150,000 ordinary shares to the number of ordinary shares reserved for issuance under the 2018 Plan.

On June 23, 2021, at the Company's annual general meeting of shareholders, the shareholders approved an amendment to the Amended and Restated 2018 Plan to increase the number of ordinary shares reserved for issuance under the amended and restated 2018 Plan by 1,000,000 ordinary shares to 1,295,819 ordinary shares.

On November 24, 2021, the Company's Board of Directors adopted and approved the 2021 Inducement Equity Incentive Plan (the 2021 Inducement Plan) reserving 333,333 of its ordinary shares to be used exclusively for grants of awards to individuals that were not previously employees or directors of the Company (or following such individuals' bona fide period of non-employment with the company), as a material inducement to such individuals' entry into employment with the company within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The terms and conditions of the 2021 Inducement Plan are substantially similar to the 2018 Plan.

Share Options

Unless specified otherwise in an individual option agreement, share options granted under the 2015 Plan, the 2018 Plan and the 2021 Inducement Plan generally have a ten year term and a three or four year vesting period for employees and a one year vesting period for directors. 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 are estimated using the Black-Scholes option-pricing model. The inputs for the Black-Scholes model require significant management assumptions. The risk-free interest rate is based on a normalized estimate of the 7-year U.S. treasury yield. The Company has estimated the expected term utilizing the "simplified" method for awards that qualify as "plain vanilla". The Company does not have sufficient company-specific historical and implied volatility information and it therefore estimates its expected share volatility based on historical volatility information of reasonably comparable guideline public companies and itself. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price. Expected dividend yield is based on the fact that the Company has never paid cash dividends and the Company's future ability to pay cash dividends on its shares may be limited by the terms of any future debt or preferred securities. The Company has elected to account for forfeitures as they occur.

The Company did not grant any share options to employees and directors during the year ended December 31, 2024 and 857,500 and 197,085 share options were granted to employees and directors during the years ended December 31, 2023 and 2022, respectively. There were 307,908, 930,010 and 296,199 unvested employee and director options outstanding as of December 31, 2024, 2023 and 2022, respectively. Total expense recognized related to the employee and director share options was $368, $468, and $3,580, for the years ended December 31, 2024, 2023 and 2022, respectively. Total unamortized compensation expense related to employee and director share options was $268, $1,000 and $929 as of December 31, 2024, 2023 and 2022, respectively, expected to be recognized over a remaining weighted average vesting period of 1.24 years, 2.09 years and 1.41 years as of December 31, 2024, 2023 and 2022, respectively.

On July 7, 2022, certain of the Company's executive officers and employees agreed to the surrender and cancellation of certain previously granted share options for an aggregate of 906,800 ordinary shares in order to make additional shares available under the 2018 Plan. Total expense recognized in connection with the cancellation of these employee share options was $17,350 for the year ended December 31, 2022, and was recorded in other income and expense as Cancellation of Share Options.

The range of assumptions that the Company used to determine the grant date fair value of employee and director options granted were as follows:

	Year Ended December 31,	
	2023	2022
Volatility	100%	100 - 130%
Expected term in years	6.00 - 6.25	5.50 - 6.25
Dividend rate	0%	0%
Risk-free interest rate	3.55% - 3.67%	1.90 - 3.96%
Share price	$1.00 - $1.04	$0.81-$6.72
Fair value of option on grant date	$0.80 - $0.84	$0.64-$5.95

The following table summarizes total stock option activity for all Company plans:

	Equity Plans	Inducement Plan	Total
Options outstanding December 31, 2021	948,639	120,000	1,068,639
Granted	190,753	6,332	197,085
Exercised	—	—	—
Forfeited	—	(3,333)	(3,333)
Cancelled Shares	(906,800)	—	(906,800)
Expired	—	—	—
Options outstanding December 31, 2022	232,592	122,999	355,591
Granted	855,000	2,500	857,500
Exercised	—	—	—
Forfeited	(103,437)	(666)	(104,103)
Expired	—	—	—
Options outstanding December 31, 2023	984,155	124,833	1,108,988
Granted	—	—	—
Exercised	(87,333)	—	(87,333)
Forfeited	(59,935)	(120,000)	(179,935)
Expired	—	—	—
Options outstanding December 31, 2024	836,887	4,833	841,720

The following table summarizes the total number of options outstanding and the weighted-average exercise price:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value (in thousands)
Options outstanding December 31, 2021	1,068,639	$ 30.12	9.42	—
Granted	197,085	$ 2.88		
Exercised	—			
Forfeited	(3,333)	$ 6.15		
Cancelled Shares	(906,800)	$ 33.16		
Expired	—			
Options outstanding December 31, 2022	355,591	$ 7.49	9.12	—
Granted	857,500	$ 1.00		
Exercised	—			
Forfeited	(104,103)	$ 2.08		
Expired	—			
Options outstanding December 31, 2023	1,108,988	$ 2.73	8.94	$ 832
Granted	—			
Exercised	(87,333)	$ 1.00		
Forfeited	(179,935)	$ 5.30		
Expired	—			
Options outstanding December 31, 2024	841,720	$ 2.37	7.76	$ 549
Exercisable at December 31, 2024	533,812	$ 3.10	7.50	$ 314

The aggregate intrinsic value of share options is calculated as the difference between the exercise price of the share options and the fair value of the Company's ordinary shares for those share options that had exercise prices lower than the fair value of the Company's ordinary shares as of December 31, 2024, 2023 and 2022, respectively.

The weighted average grant-date fair value per share of share options granted during the years ended December 31, 2023 and 2022 was $0.80 and $2.39, respectively.

Restricted Share Units (RSUs)

No RSUs were granted to employees or directors during the years ended December 31, 2024 and 2023. The Company granted 66,398 RSUs to employees and directors during the year ended December 31, 2022.

The following table summarizes the number of RSUs granted covering an equal number of the Company's ordinary shares for all of our plans:

	Equity Plans	Inducement Plan	Total
RSUs outstanding December 31, 2021	85,684	33,333	119,017
Granted	66,398	—	66,398
Shares vested	(48,353)	(8,334)	(56,687)
Forfeited	—	—	—
RSUs outstanding December 31, 2022	103,729	24,999	128,728
Granted	—	—	—
Shares vested	(103,729)	(8,333)	(112,062)
Forfeited	—	—	—
RSUs outstanding December 31, 2023	—	16,666	16,666
Granted	—	—	—
Shares vested	—	—	—
Forfeited	—	(16,666)	(16,666)
RSUs outstanding December 31, 2024	—	—	—

The table below shows the total number of RSUs granted and the weighted-average grant date fair value of the total RSUs granted:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
RSUs outstanding December 31, 2021	119,017	$ 19.16
Granted	66,398	$ 2.91
Shares vested	(56,687)	$ 21.23
Forfeited	—	
RSUs outstanding December 31, 2022	128,728	$ 9.87
Granted	—	
Shares vested	(112,062)	$ 10.26
Forfeited	—	
RSUs outstanding December 31, 2023	16,666	$ 7.26
Granted	—	
Shares vested	—	
Forfeited	(16,666)	$ 7.26
RSUs outstanding December 31, 2024	—	

The fair value of the RSUs is determined on the date of grant based on the market price of the Company's ordinary shares on that date. The fair value of RSUs is expensed ratably over the vesting period, which is generally one year for directors and two years for employees under our 2018 Plan and four years for employees under our 2021 Inducement Plan. Total benefit recognized related to the RSUs was $5 for the year ended December 31, 2024, and total expense recognized related to the RSUs was $316 and $1,178 for the years ended December 31, 2023 and 2022, respectively. There was no unamortized compensation expense related to the RSUs as of December 31, 2024, and total unamortized compensation expense related to the RSUs was $116 and $434 as of December 31, 2023 and 2022, respectively, which was expected to be recognized over a remaining average vesting period of 1.92 years and 0.88 years as of December 31, 2023 and 2022, respectively.

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

	Year ended December 31,		
	2024	2023	2022
Research and development expense	$ 193	$ 412	$ 1,396
General and administrative expense	170	372	3,362

There was a total of $268, $1,116 and $1,363 unamortized share-based compensation expense for share options and restricted share units as of December 31, 2024, 2023 and 2022, respectively, expected to be recognized over a remaining average vesting period of 1.24 years, 2.07 years and 1.28 years as of December 31, 2024, 2023 and 2022, respectively.

(15)Income Taxes

During the years ended December 31, 2024, 2023 and 2022, the Company recorded no income tax benefits for the net operating losses incurred in each year due to its uncertainty of realizing a benefit from those items.

The provision for income taxes consists of the following components:

	Year Ended December 31,		
	2024	2023	2022
Current			
U.S.	$ 240	$ 613	$ 301
Ireland	—	—	—
Total Current	$ 240	$ 613	$ 301
Deferred			
U.S.	$ —	$ —	$ —
Ireland	—	—	—
Total Deferred	$ —	$ —	$ —
Income Tax Provision	$ 240	$ 613	$ 301

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

	Year Ended December 31,		
	2024	2023	2022
U.S.	$ 370	$ 1,743	$ (13,701)
Ireland	(24,904)	(39,501)	(30,432)
Total	$ (24,534)	$ (37,758)	$ (44,133)

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

	Year Ended December 31, 2024		Year Ended December 31, 2023		Year Ended December 31, 2022	
Statutory rate	12.50%	$ (3,067)	12.50%	$ (4,720)	12.50%	$ (5,517)
Impact of U.S. tax rate	0.23%	(57)	0.72%	(272)	4.71%	(2,080)
Impact of valuation allowance	(12.27)%	3,012	(14.48)%	5,466	(5.30)%	2,341
Adjustments for current tax of prior periods	2.13%	(522)	0.14%	(52)	(4.19)%	1,851
Cancellation of share options	0.00%	—	0.00%	—	(9.02)%	3,983
Fair value movements on derivative financial instruments	(2.53)%	621	3.66%	(1,382)	1.55%	(682)
Other, net	(1.03)%	253	(4.17)%	1,573	(0.92)%	405
Effective tax rate	(0.98)%	$ 240	(1.62)%	$ 613	(0.68)%	$ 301

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

	Year Ended December 31,		
	2024	2023	2022
Deferred tax assets			
Share-based compensation	$ 73	$ 154	$ 438
Depreciation	1	45	42
Net operating loss carryforwards	44,536	41,525	36,059
Other	4	4	(11)
Valuation allowance	(44,614)	(41,728)	(36,528)
Total deferred tax assets	$ —	$ —	$ —
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 of approximately $44,536, $41,525 and $36,059 as of the years ended December 31, 2024, 2023 and 2022, 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:

	2024	2023
Balance at January 1	$ 2,020	$ 2,844
Decrease in tax positions	(111)	(824)
Balance at December 31	$ 1,909	$ 2,020

The Company's federal and state income tax returns for 2021 through 2023 remain open to examination by the IRS. The Company's income tax returns in Ireland remain open to examination from 2020 to 2023. The Company is not currently subject to any audits or examination.

In August 2022, the Inflation Reduction Act of 2022 (IRA) was signed into law in the United States. The IRA created a new corporate alternative minimum tax of 15% on adjusted financial statement income and an excise tax of 1% of the value of certain stock repurchases. The provisions of the IRA will be effective for periods beginning after December 31, 2022. The enactment of the IRA did not result in any material adjustments to the Company's income tax provisions or net deferred tax assets as of December 31, 2024.

(16)Commitments and Contingencies

License Agreement

On November 18, 2015, the Company and ITIL, entered into the Pfizer License.

Under the Pfizer License, the Company is obligated to make a potential one-time payment related to sublicensing income that exceeds a certain threshold. The Company is obligated to pay Pfizer potential future regulatory milestone payments, as well as sales milestones upon achievement of net sales ranging from $250.0 million to $1.0 billion for each product type. The Company is also obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage based on marginal net sales of each licensed product.

Royalty-Linked Notes

On January 21, 2020, as part of the Private Placement, the Company issued 2,579,400 RLNs to a group of accredited investors. On September 8, 2020, as part of the Rights Offering, the Company issued 11,000 RLNs to existing shareholders. The RLNs will entitle the holders thereof to payments, at the applicable payment rate, based solely on a percentage of the Company’s net revenues from U.S. sales of specified sulopenem products earned through December 31, 2045, but will not entitle the holders thereof to any payments unless the Company receives FDA approval for one or more specified sulopenem products prior to December 31, 2025 and the Company earns net revenues on such product. If any portion of the principal amount of the outstanding RLNs, equal to $0.04 per RLN, has not been paid as of the end date on December 31, 2045, Iterum Bermuda must pay the unpaid portion of the principal amount. The RLNs will earn default interest if the Company breaches certain obligations under the RLN Indenture (but do not otherwise bear interest) and will be subject to a maximum return amount, including all principal and payments and certain default interest in respect of uncurable defaults, of $160.00 (or 4,000 times the principal amount of such note). The RLNs will be redeemable at the Company’s option, subject to the terms of the RLN Indenture.

Other 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 has no contingent liabilities in respect of legal claims arising in the ordinary course of business.

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” (other than due to death or disability) or upon “resignation for good reason”, contingent upon the named executive officer’s continued performance for the Company. Under the terms of the Employee Severance Plan approved by the Compensation Committee in January 2022, an employee, who is not an executive officer

of the Company, is entitled to severance pay and benefits on a "qualifying termination", that is termination at any time during the period beginning on the date that is 30 days prior to and ending on the date that is 12 months following a change of control without "cause" (other than due to death or disability) based on the employee's level/salary grade.

(17)Condensed Consolidating Financial Statements

On January 21, 2020, the Company completed a Private Placement pursuant to which its wholly owned subsidiary, Iterum Bermuda, issued and sold $51,588 aggregate principal amount of Exchangeable Notes and $103 aggregate principal amount of RLNs to a group of accredited investors. On September 8, 2020, the Company completed a Rights Offering pursuant to which Iterum Bermuda issued and sold $220 aggregate principal amount of Exchangeable Notes and $0.44 aggregate principal amount of RLNs to existing shareholders. The Securities were sold in Units with each Unit consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs. As of December 31, 2024, $11,117 aggregate principal amount of Exchangeable Notes and all RLNs remained outstanding. See Note 18 – Subsequent Events for details of repayment of the Exchangeable Notes in January 2025.

The Units were issued by Iterum Bermuda, which was formed on November 6, 2019 and is a 100% owned “finance subsidiary” of the Company under Rule 3-10 of Regulation S-X with no independent function and no assets or operations other than those related to the issuance, administration and repayment of the Exchangeable Notes and RLNs. Iterum Therapeutics plc, as the parent company, has no independent assets or operations, and its operations are conducted solely through its subsidiaries. The assets, liabilities and results of operations of the Company, Iterum Bermuda and Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited (the Subsidiary Guarantors) are not materially different than the corresponding amounts presented in the consolidated financial statements of this Annual Report on Form 10-K. The Company and the Subsidiary Guarantors have provided a full and unconditional guarantee of Iterum Bermuda’s obligations under the Exchangeable Notes and the RLNs, and each of the guarantees constitutes the joint and several obligations of the applicable guarantor. The Subsidiary Guarantors are 100% directly or indirectly owned subsidiaries of the Company. There are no significant restrictions upon the Company’s or the Subsidiary Guarantors’ ability to obtain funds from their subsidiaries by dividend or loan. None of the assets of Iterum Bermuda or the Subsidiary Guarantors represent restricted net assets pursuant to Rule 4-08(e)(3) of Regulation S-X.

(18) Subsequent Events

Exchangeable Notes Repayment

On January 31, 2025, the Exchangeable Notes matured and Iterum Bermuda repaid to the holders thereof an aggregate principal amount of $11,117 together with accrued interest of $3,628.

Equity

Subsequent to December 31, 2024, through February 6, 2025, the Company sold 3.0 million ordinary shares under the Sales Agreement, with HC Wainwright as agent, at an average price of $1.64 per share for net proceeds of $4,827.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2024. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2024, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), we conducted an evaluation of the effectiveness of our internal control over financial reporting. We used the 2013 framework in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission to evaluate the effectiveness of our internal control over financial reporting. Based on our evaluation under that framework, our management has concluded that our internal control over financial reporting was effective as of December 31, 2024.

Our independent registered public accounting firm has not performed an evaluation of our internal control over financial reporting during any period in accordance with the provisions of the Sarbanes-Oxley Act. For as long as we remain a "smaller reporting company" as defined in Rule 12b-2 promulgated under the Exchange Act, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting. We may remain a smaller reporting company until we have a non-affiliate public float in excess of $250 million and annual revenues in excess of $100 million, or a non-affiliate public float in excess of $700 million, each as determined on an annual basis.

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the quarter ended December 31, 2024, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Trading Arrangements

During the three months ended December 31, 2024, no director or officer of the Company adopted or terminated a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement", as each term is defined in Item 408(a) of Regulation S-K.

We have adopted an Insider Trading and Trading Window Policy governing the purchase, sale, and other dispositions of our securities by directors, officers and employees, that are reasonably designed to promote compliance with insider trading laws, rules and regulations, and any applicable listing standards.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Directors

The following table sets forth information regarding our directors as of January 31, 2025.

Name	Age	Position
Corey N. Fishman	60	Director, President and Chief Executive Officer
Michael W. Dunne	65	Director
Beth P. Hecht [(1)(2)]	61	Director
Ronald M. Hunt [(1)(2)(3)]	60	Director
David G. Kelly [(2)(3)]	63	Director

(1) Member of the compensation committee

(2) Member of the audit committee

(3) Member of the nominating and corporate governance committee

Corey N. Fishman has served as our President and Chief Executive Officer and as a 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 (Actavis), a pharmaceutical company, and he also served as chief financial officer of Durata Therapeutics, Inc., from June 2012 to February 2015. From 2008 to 2010, Mr. Fishman served as chief financial officer of GANIC Pharmaceuticals, Inc., a pharmaceutical company. From 2002 to 2008, Mr. Fishman served in a variety of roles at MedPointe Healthcare, Inc., a specialty pharmaceutical company acquired by Meda AB, including as chief financial officer from 2006 to 2008. Mr. Fishman previously served on the board of directors of Momenta Pharmaceuticals, Inc., a biotechnology company, from September 2016 until June 2020 and BioSpecifics Technology Corporation, a biopharmaceutical company, from April 2020 until its acquisition by Endo International plc in December 2020. 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 has served as a member of our board of directors since December 2020 and serves as a consultant for one of our wholly owned subsidiaries since December 2020. From December 2020 until January 2025, Dr. Dunne served as the chief medical officer at the Gates Medical Research Institute. Previously, Dr. Dunne served as our chief scientific officer from November 2015 to December 2020. From November 2014 until September 2015, Dr. Dunne was vice president of research and development at Actavis. From September 2010 to October 2014, Dr. Dunne served as chief medical officer of Durata Therapeutics, Inc., where he previously served as acting chief medical officer on a consulting basis from December 2009 to September 2010. From 1992 to 2009, Dr. Dunne served in a variety of roles in connection with the clinical development of numerous infectious disease compounds at Pfizer Inc., a biopharmaceutical company, including as the vice president, therapeutic area head of development for infectious disease from 2001 to 2009. Dr. Dunne served as a member of the board of directors of Aviragen Therapeutics, Inc, a biotechnology company from 2015 to 2018. 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. We believe Dr. Dunne is qualified to serve on our board of directors due to his role as co-founder of the Company, his deep knowledge of our Company and his extensive background and medical experience in infectious disease.

Beth P. Hecht has served as a member of our board of directors since March 2021. Since October 2021, Ms. Hecht has served as chief legal officer and corporate secretary of Xeris Biopharma Holdings Inc., a specialty pharmaceutical company. From January 2019 to October 2021, Ms. Hecht served as senior vice president, general counsel and corporate secretary of Xeris Pharmaceuticals, Inc., a specialty pharmaceutical company. From October 2012 to December 2018, Ms. Hecht served as managing director and chief legal and administrative officer for Auven Therapeutics Management L.L.P., a global biotechnology and pharmaceutical private equity firm. Ms. Hecht previously served on the board of directors of Neos Therapeutics, Inc. a pharmaceutical company, from September 2015 until its acquisition by Aytu BioPharma Inc., formerly Aytu Bioscience, Inc., in March 2021 and also served on the board of directors of Aytu BioScience Inc. from March 2021 until May 2021. Ms. Hecht is a graduate of Amherst College and Harvard Law School and started her career as an attorney specializing in intellectual property and corporate transactions at Willkie Farr & Gallagher (New York) and then Kirkland & Ellis (New York). We believe Ms. Hecht is qualified to serve on our board of directors due to her extensive experience in the pharmaceutical industry and her service on the boards of directors of other pharmaceutical companies.

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 as a partner at the Sprout Group, a venture capital firm, and was a consultant with consulting firms Coopers & Lybrand Consulting and The Health

Care Group. Mr. Hunt also previously served in various sales and marketing positions at Johnson & Johnson and SmithKline Beecham Pharmaceuticals. Mr. Hunt currently serves as a board member of Rallybio Corporation, a clinical-stage biotechnology company, and on the boards of a number of private pharmaceutical and healthcare companies. Mr. Hunt previously served on the board of directors of Harpoon Therapeutics, Inc., from 2017 to March 2024 and Neuronetics, Inc. from 2015 to May 2019. Mr. Hunt holds a B.S. from Cornell University and an M.B.A. from the Wharton School of the University of Pennsylvania. We believe Mr. Hunt is qualified to serve on our board of directors due to his investment experience, his experience in the pharmaceuticals industry and his service on the boards of directors of other biopharmaceutical companies.

David G. Kelly has served as a member of our board of directors since August 2016. From September 2014 to January 2020, Mr. Kelly served as the executive vice president, Ireland of Horizon Therapeutics, plc, a biopharmaceutical company. Mr. Kelly served as managing director, Ireland of Horizon Therapeutics, plc until July 2018. From February 2012 to September 2014, Mr. Kelly served as chief financial officer of Vidara Therapeutics Inc., a pharmaceutical company. From May 2005 to January 2012, Mr. Kelly served as chief financial officer of AGI Therapeutics plc, a pharmaceutical company. Mr. Kelly also served as senior vice president, finance and planning of Warner Chilcott plc (formerly Galen Holdings plc), a pharmaceutical company listed on the London Stock Exchange (LSE). In addition, Mr. Kelly held roles at Elan Corporation, a pharmaceutical company, and KPMG. Mr. Kelly holds a B.A. in economics from Trinity College, Dublin and is also a member of the Institute of Chartered Accountants in Ireland (ACA). We believe Mr. Kelly is qualified to serve on our board of directors due to his experience as a senior executive, particularly within the life science industry, including his experience in finance.

Executive Officers

The following table sets forth information regarding our executive officers as of January 31, 2025.

Name	Age	Position
Corey N. Fishman	60	Director, President and Chief Executive Officer
Judith M. Matthews	55	Chief Financial Officer

In addition to the biographical information for Mr. Fishman, which is set forth above, set forth below is certain biographical information about Ms. Matthews:

Judith M. Matthews has served as our Chief Financial Officer since November 2015. From 2012 to February 2015, Ms. Matthews served as vice president of finance at Durata Therapeutics, Inc. From 2009 to 2012, Ms. Matthews served as head of financial planning & analysis at Bally Total Fitness Corporation, a fitness club chain. From 2004 to 2008, Ms. Matthews served as vice president of finance for the Sterno Group, a subsidiary of Blyth, Inc., a home products company. Ms. Matthews holds a B.A. in accounting from the University of Illinois at Urbana-Champaign and a Master of Management in finance and marketing from the Kellogg School of Management at Northwestern University.

Committees of our Board of Directors

Our board of directors has established an audit committee, a compensation committee, and a nominating and corporate governance committee, each of which operates under a charter that has been approved by our board of directors. The charters for each of these committees are available on our website at www.iterumtx.com.

Audit Committee

Our audit committee consists of David G. Kelly (Chairman), Beth P. Hecht and Ronald M. Hunt. The chairperson of our audit committee is Mr. Kelly.

Our board of directors has determined that Messrs. Kelly and Hunt and Ms. Hecht each satisfy the independence standards for such committees established by the U.S. Securities and Exchange Commission (SEC) and the Nasdaq Stock Market.

Our board of directors has determined that Mr. Kelly is an “audit committee financial expert” within the meaning of SEC regulations. Our board of directors has also determined that each member of our audit committee has the requisite financial expertise required under the applicable requirements of the Nasdaq Stock Market. In arriving at this determination, the board of directors has examined each audit committee member’s scope of experience and the nature of their employment in the corporate finance sector.

Code of Business Conduct and Ethics

We have adopted a written Code of Business Conduct and Ethics that applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The Code of Business Conduct and Ethics is available on our website at www.iterumtx.com. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website or in a Current Report on Form 8-K.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors and executive officers, and holders of more than ten percent of our ordinary shares, to file with the SEC initial reports of ownership of our ordinary shares and other equity securities and reports of changes in ownership of our ordinary shares and other equity securities. Such executive officers, directors and holders of more than ten percent of our ordinary shares are required by SEC regulations to furnish us with copies of all Section 16(a) forms they file.

To our knowledge, based solely on a review of the copies of such reports furnished to us and written representations regarding the filing of required reports, we believe that all Section 16(a) filing requirements applicable to our directors, executive officers and holders of more than ten percent of our ordinary shares, with respect to fiscal year ended December 31, 2024, were met except for three reports on Form 4 for each of Mr. Hunt, Dr. Dunne and Mr. Fishman, in each case disclosing the director's exercise of subscription rights to acquire ordinary shares of the Company and warrants to purchase ordinary shares of the Company on August 6, 2024 as part of the rights offering that was completed on August 9, 2024.

Insider Trading and Trading Window Policy

We have adopted an Insider Trading and Trading Window Policy governing the purchase, sale, and other dispositions of our securities by directors, officers and employees, as well as us, that are reasonably designed to promote compliance with insider trading laws, rules and regulations, and any applicable listing standards of The Nasdaq Stock Market LLC.

Involvement in Certain Legal Proceedings

We are not aware of any of our directors or executive officers being involved in any legal proceeding in the past ten years relating to any matters in bankruptcy, insolvency, criminal proceedings (excluding traffic and other minor offenses), or being subject to any of the items set forth under Item 401(f) of Regulation S-K.

Item 11. Executive Compensation.

The following discussion provides details of the compensation and other benefits paid by us and our subsidiaries to certain executive officers for services provided for the years ended December 31, 2024 and 2023 and to the members of our board of directors for services provided for the year ended December 31, 2024.

Executive and Director Compensation Processes

Our executive compensation program is administered by our compensation committee, subject to oversight by our board of directors. Our compensation committee reviews our executive compensation practices on an annual basis and approves, or recommends for approval by the board, the compensation of the Company’s executives.

Our compensation committee periodically reviews and makes recommendations to the board of directors with respect to director compensation. As and when required, we have retained the services of Coda Advisors LLC (Coda), as an independent compensation consultant to provide comparative data on executive compensation practices in our industry and to provide advice to the compensation committee in relation to our executive compensation program. While Coda has provided advice to the Company and the compensation committee in relation to such compensation practices from time to time, the compensation committee ultimately makes its own decisions with regard to our executive and director compensation programs.

Executive Officer Summary Compensation Table

The following table provides details of the compensation and other benefits paid or accrued by us and our subsidiaries to our named executive officers for the year ended December 31, 2024, who are our President and Chief Executive Officer, Corey N. Fishman, and our two next most highly compensated executive officers, Dr. Sailaja Puttagunta, our former Chief Medical Officer, and Ms. Judith M. Matthews, our Chief Financial Officer:

Name and Principal Position	Year Ended December 31,	Salary ($)	Bonus[1] ($)	Share Awards ($)	Option Awards[2] ($)	Non-Equity Incentive Plan Compensation[3] ($)	All Other Compensation ($)	Total ($)
Corey N. Fishman	2024	630,678	146,073	—	—	347,716	8,549 (4)	1,133,016
President and Chief Executive Officer	2023	611,831	360,311	—	220,000	320,709	5,960 (4)	1,518,811
Sailaja Puttagunta	2024	325,301(4)	12,825	—	—	—	2,470 (5)	340,596
Chief Medical Officer	2023	492,417	237,263	—	60,000	211,185	5,960 (4)	1,006,825
Judith M. Matthews	2024	429,550	71,400	—	—	172,438	3,647 (4)	677,035
Chief Financial Officer	2023	411,211	176,120	—	80,000	156,763	3,680 (4)	827,774

(1) The amounts reported in the "Bonus" column for Mr. Fishman, Ms. Matthews and Dr. Puttagunta during 2024 and 2023 reflect certain discretionary cash bonuses to incentivize the continued dedication of executives which were expensed in the relevant period.
(2) The amounts reported do not reflect the amounts actually received by our executive officers. Instead, these amounts reflect the aggregate grant date fair values of share options granted to each of our executive officers during the year ended December 31, 2023 as computed in accordance with Financial Accounting Standards Board (FASB), Accounting Standards Codification (ASC) 718. Assumptions used in the calculation of these amounts are included in Note 14 to our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2023. 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 share options will only realize compensation with regard to these share options to the extent the trading price of our ordinary shares is greater than the exercise price of such share options and such share options vest.
(3) Amount represents cash bonuses earned for the 12-month periods ending December 31, 2024 and 2023, respectively. Amounts disclosed for the year ended December 31, 2024 exclude payments made in 2024 for 2023 bonuses. Amounts disclosed for the year ended December 31, 2023 exclude payments made in 2023 for 2022 bonuses.
(4) Includes (i) salary of $224,901 paid to Dr. Puttagunta prior to departure in May 2024; and (ii) consulting fees of $100,400 incurred in connection with Dr. Puttagunta's consulting arrangement entered into with our subsidiary, Iterum Therapeutics International Limited (ITIL), dated May 29, 2024.
(5) Includes the dollar value of life insurance premiums paid by the company for the benefit of such executive officer.

Narrative Disclosure to Executive Officer Summary Compensation Table

Base Salary

During the year ended December 31, 2024, we paid base salaries of $632,212 to Mr. Fishman and $431,097 to Ms. Matthews.

Dr. Puttagunta resigned from the Company effective May 31, 2024. Prior to Dr. Puttagunta's resignation, she was entitled to a base salary of $516,230 of which we paid $224,901 prior to her departure. During the year ended December 31, 2023, we paid annualized base salaries of $613,798 to Mr. Fishman, $494,000 to Dr. Puttagunta and $412,533 to Ms. Matthews.

In February 2025, our compensation committee approved an increase to the annualized based salaries of our executive officers, effective February 1, 2025, as follows: $648,017 to Mr. Fishman and $446,185 to Ms. Matthews.

None of the named executive officers were or are currently party to any employment arrangements that provide for automatic or scheduled increases in base salary.

Non-Equity Incentive Plan Compensation

Our named executive officers participate in a cash bonus program which is tied to the achievement of strategic and corporate goals of the Company, which are approved annually by our compensation committee. Our compensation committee determines the amount of these bonuses, if any, based on its assessment of the named executive officers' performance and that of the Company against goals established annually.

Under their respective employment agreements, the annual target bonus for Mr. Fishman is 55% of his current base salary, the annual target bonus for Dr. Puttagunta was 45% of her current base salary and the annual target bonus for Ms. Matthews is 40% of her current base salary.

At the beginning of each year, our compensation committee reviews the accomplishments of the named executive officers as measured against the previous year's goals, whether each goal had been achieved and the relative weight that should be given to each goal in determining the cash bonus payment for that year. Based on its review, our compensation committee recommended cash bonus payments of $347,716 to Mr. Fishman and $172,438 to Ms. Matthews with respect to the year ended December 31, 2024. Our compensation committee recommended cash bonus payments of $320,709 to Mr. Fishman, $211,185 to Dr. Puttagunta and $156,763 to Ms. Matthews with respect to the year ended December 31, 2023.

Bonuses

No special bonus payments were recommended for executives in 2024 .

During 2023, the compensation committee also recommended special retention bonus payments for executives of $506,383 to Mr. Fishman, $333,450 to Dr. Puttagunta and $247,520 to Ms. Matthews payable on the achievement of certain milestones to incentivize the continued dedication of executives, of which we paid $506,383 to Mr. Fishman and $247,520 to Ms. Matthews during 2024. $166,725 was paid to Dr. Puttagunta on the achievement of certain milestones prior to her departure in May 2024.

Equity Incentive Awards

We believe that our ability to grant equity-based awards is a valuable and necessary compensation tool that aligns the long-term financial interests of our executive officers and our shareholders. In addition, we believe that our ability to grant share options and other equity-based awards helps us to attract, retain and motivate our executive officers and encourages them to devote their best efforts to our business and financial success.

No equity-based awards were granted to executives in 2024.

In January 2023, the compensation committee approved the grant of share options under the 2018 Plan to Mr. Fishman, Dr. Puttagunta and Ms. Matthews to purchase the following number of ordinary shares, which grants will become effective as of March 31, 2023: 275,000 to Mr. Fishman, 75,000 to Dr. Puttagunta; and 100,000 to Ms. Matthews (the 2023 Share Options). Such share options vested as to 33.33% of the ordinary shares underlying such share options on the first anniversary of the date of grant based on each such named executive officer's continued service with us through that date and the remaining ordinary shares vesting in 24 equal monthly installments thereafter subject to each such named executive officer's continued provision of services to us on each vesting date. The compensation committee also approved that in the event of a change of control, the vesting and exercisability of any then-unvested 2023 Share Options held by each of Mr. Fishman, Dr. Puttagunta and Ms. Matthews, will be accelerated in full.

Consulting Agreement - Sailaja Puttagunta, M.D.

During 2024, we compensated Sailaja Puttagunta, M.D., our former chief medical officer pursuant to a consulting agreement entered into with our subsidiary, ITIL, dated May 29, 2024, (the Puttagunta Consulting Agreement), effective June 1, 2024. The Puttagunta Consulting Agreement entitles Dr. Puttagunta to consulting fees of $400 per hour for the provision of general support in connection with our New Drug Application (NDA) for oral sulopenem to the U.S. Food and Drug Administration. An aggregate of $100,400 was expensed for services provided by Dr. Puttagunta during the fiscal year ended December 31, 2024 pursuant to the Puttagunta Consulting Agreement.

Outstanding Equity Awards at December 31, 2024

The following table presents information regarding outstanding equity awards held by our named executive officers as of December 31, 2024. All equity awards were granted under our 2015 Equity Incentive Plan (2015 Plan), our 2018 Equity Incentive Plan (2018 Plan) and our 2021 Inducement Equity Incentive Plan (2021 Inducement Plan):

	Option Awards				Share Awards	
Name	**Number of Securities Underlying Unexercised Options (#) Exercisable**	**Number of Securities Underlying Unexercised Options (#) Unexercisable** (1)	**Option Exercise Price Per Share ($)** (2)	**Option Expiration Date**	**Equity incentive plan awards: Number of unearned shares, units or other rights that have not vested (#)**	**Equity incentive plan awards: Market or payout value of unearned shares, units or other rights that have not vested ($)**
Corey N. Fishman	4,356 (3)	—	$ 49.50	09/11/2027	—	—
	160,359	114,641 (4)	$ 1.00	03/31/2031	—	—
Judith M. Matthews	792 (3)	—	$ 49.50	09/11/2027	—	—
	58,313	41,687 (4)	$ 1.00	03/31/2031	—	—

(1) Pursuant to the equity agreements between the named executive officer and us, the vesting of such named executive officer's share and option awards will accelerate under certain circumstances as described under the section titled "—Potential Payments Upon Termination or Change in Control" below.
(2) The exercise price per share of the share options reflects the fair market value per ordinary share on the date of grant.
(3) Share option that vested as to 25% of the ordinary shares underlying the share option on September 12, 2018, with the remaining ordinary shares vesting in equal monthly installments thereafter until September 12, 2021.
(4) Share option that vest as to 33% of the ordinary shares underlying the share option on March 31, 2024, with the remaining ordinary shares vesting in equal monthly installments thereafter until March 31, 2026, subject to continued service with us through each relevant vesting date.

Employment Agreements with Executive Officers

We have entered into offer letters with each of our named executive officers. The offer letters generally provide for at-will employment and set forth the executive's initial base salary, target variable compensation, eligibility for employee benefits, the terms of initial equity grants and severance benefits on a qualifying termination. Each of our named executive officers has also executed our standard form proprietary information agreement. Any potential payment and benefits due upon a termination of employment or change of control of us are further described below.

Corey N. Fishman serves as our President and Chief Executive Officer. On November 18, 2015, Mr. Fishman entered into an offer letter with Iterum Therapeutics US Limited, our indirect wholly owned subsidiary. The offer letter has no specific term and constitutes an at-will employment arrangement. On May 2, 2018, Mr. Fishman entered into an amended offer letter, which became effective upon the closing of our initial public offering pursuant to which Mr. Fishman's base salary became $540,000, and his discretionary annual target performance bonus increased from 50% to 55% of his annual base salary. His base salary was reviewed in December 2020 and increased to $573,000, effective January 1, 2021. His base salary was reviewed in January 2022 and increased to $590,190, effective February 1, 2022. His base salary was reviewed in January 2023 and increased to $613,798, effective February 1, 2023. His base salary was reviewed in January 2024 and increased to $632,212, effective February 1, 2024.

Judith M. Matthews serves as our Chief Financial Officer. On November 18, 2015, Ms. Matthews entered into an offer letter with Iterum Therapeutics US Limited, our indirect wholly owned subsidiary. The offer letter has no specific term and constitutes an at-will employment arrangement. Ms. Matthews entered into an amended offer letter, which became effective upon the closing of our initial public offering pursuant to which Ms. Matthews' base salary became $350,000, and her discretionary annual target performance bonus increased from 25% to 35% of her annual base salary. In January 2022 our compensation committee approved an increase in Ms. Matthew's annual target performance bonus to 40%. Ms. Matthew's base salary was reviewed in December 2020 and increased to $381,410, effective January 1, 2021. Her base salary was reviewed in January 2022 and increased to $396,666, effective February 1, 2022. Her base salary was reviewed in January 2023 and increased to $412,533, effective February 1, 2023. Her base salary was reviewed in January 2024 and increased to $431,097, effective February 1, 2024.

Potential Payments Upon Termination or Change in Control

Our agreements with each of our named executive officers provide that upon the termination of his or her employment by us other than for cause (other than due to death or disability), or by the named executive officer with good reason (each as defined below), he or she will be entitled to receive the following severance benefits:

- cash severance equal to a fixed number of months of such executive officer's base salary (twelve months in the case of Mr. Fishman and nine months in the case of Ms. Matthews), payable in installments following such termination in the form of base salary continuations; and
- Company-paid COBRA premiums for up to 12 months (or 18 months for Mr. Fishman) following such executive officer's termination date.

"Cause" for termination as used in each of the offer letters means (a) commission or conviction by the named executive officer (including a guilty plea or plea of nolo contendere) of any felony or any other crime involving fraud, dishonesty or moral turpitude; (b) commission by the named executive officer or attempted commission of or participation in a fraud or act of dishonesty or misrepresentation against the Company; (c) material breach by the named executive officer of his or her duties to the Company; (d) intentional damage by the named executive officer to any property of the Company; (e) misconduct, or other violation of Company policy that causes harm; (f) material violation by the named executive officer of any written and fully executed contract or agreement between him or her and the Company; or (g) conduct by the named executive officer which, in the good faith and reasonable determination of the Company, demonstrates gross unfitness to serve. The determination that a termination is for Cause shall be made by the Company in its sole discretion.

Pursuant to each of the offer letters, the named executive officer shall have "good reason" for resigning from employment with the Company if any of the following actions are taken by the Company without his or her prior written consent: (a) a material reduction in his or her base salary, which is a reduction of at least 10% of his or her base salary (unless pursuant to a salary reduction program applicable generally to the Company's similarly situated employees); (b) a material reduction in his or her duties (including responsibilities and/or authorities), provided, however, that a change in job position (including a change in title) shall not be deemed a "material reduction" in and of itself unless his or her new duties are materially reduced from the prior duties; or (c) relocation of the name executive officer's principal place of employment to a place that increases his or her one-way commute by more than fifty (50) miles as compared to his or her then-current principal place of employment immediately prior to such relocation.

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 12 months of such executive officer's then current base salary in the case of Ms. Matthews, and to 18 months of his then current base salary in the case of Mr. Fishman. The

executives officers will also be entitled to an additional cash payment equal to a percentage of such executive officers' target annual bonus for the year of termination, equal to 100% in the case of Dr. Puttagunta and Ms. Matthews and 150% in the case of Mr. Fishman.

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 (the Code), the payments will either be (i) reduced or (ii) provided in full to the executive officer, whichever results in the executive officer 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 the equity agreements between each of the named executive officers and us, in the event of a qualifying termination in connection with a change of control, the vesting and exercisability of any then-unvested share options, restricted share unit awards or any other share awards outstanding under the 2015 Plan, the 2018 Plan and/or the 2021 Inducement Plan held by each of Mr. Fishman, Dr. Puttagunta and Ms. Matthews, will be accelerated in full.

On March 11, 2020, on recommendation from the compensation committee, our board of directors approved the creation of a carve out plan to reward certain key employees including Mr. Fishman and Ms. Matthews in the event of a change of control. The aggregate amount payable under the plan will be calculated on a tiered basis based on the upfront consideration payable to us and our ordinary shareholders in connection with such change of control, with potential aggregate amounts payable under the plan falling within a range around approximately 2.5% of the upfront consideration. The other terms of the plan and each executive officer's entitlement to participate are to be determined at the time of the change of control transaction.

Director Compensation – Summary Compensation Table

The following table shows the total compensation paid or accrued by us and our subsidiaries during the year ended December 31, 2024, to each of our current non-employee directors. Directors who are employed by us are not compensated for their service on our board of directors.

Name	Fees Earned or Paid in Cash ($)	Share Awards ($) (1)	Option Awards ($) (2)	All Other Compensation ($)	Total ($)
Michael Dunne, M.D.	75,000 (4)	—	—	60,000 (3)	135,000
Beth P. Hecht	88,500 (4)	—	—	—	88,500
Ronald M. Hunt	130,000 (4)	—	—	—	130,000
David G. Kelly	94000 (4)	—	—	—	94,000

(1) No outstanding restricted share units were held by our non-employee directors as of December 31, 2024.
(2) No share options were granted to our non-employee directors in 2024. The aggregate number of shares subject to outstanding share options units held by each of our non-employee directors as of December 31, 2024 were as follows: Dr. Dunne 13,742; Ms. Hecht 0; Mr. Hunt: 43,886; and Mr. Kelly: 51,850
(3) Represents consulting fees of $60,000 incurred in connection with Dr. Dunne's consulting arrangement.
(4) Includes (i) annual cash retainer(s) for services on the board and committee(s) (as relevant) and/or as chairperson of the board or a committes (as relevant); and (ii) $40,000 paid to non-employee directors in lieu of annual equity awards to be made at the 2024 annual general meeting of shareholders.

In May 2023 the board of directors resolved to suspend annual equity awards due to be granted to non-employee directors pursuant to our Amended and Restated Non-Employee Director Compensation Policy and any further grants of awards pursuant to that policy to be made in lieu of cash compensation. In lieu of the annual equity award to be made at the 2024 annual general meeting of shareholders, a cash amount of $40,000 was paid to the non-employee directors.

Consulting Agreement - Michael Dunne, M.D.

During 2024, we compensated Michael Dunne, M.D., our former chief scientific officer and current member of our board of directors, pursuant to a consulting agreement entered into with our subsidiary, ITIL, dated May 25, 2022, (the Dunne Consulting Agreement), effective May 1, 2022. The Dunne Consulting Agreement entitles Dr. Dunne to consulting fees of $5,000 per month for the provision of general support and strategic advice in connection with the potential resubmission of the NDA including the design and conduct of a Phase 3 clinical trial to support such resubmission. The Dunne Consulting Agreement was amended, effective December 31, 2022, to extend the term of the Dunne Consulting Agreement by six months, or until June 30, 2023. It was further amended on June 15, 2023 to extend the term by six months, or until December 31, 2023, on December 27, 2023 to extend the term until June 30, 2024, on August 9, 2024, with an effective date of June 30, 2024, to extend the term until December 31, 2024 and on December 5, 2024 extend the term until June 30, 2025. An aggregate of $60,000 was expensed for services provided by Dr. Dunne in 2024 pursuant to the Dunne Consulting Agreement, as amended.

Non-Employee Director Compensation Policy

Under our Amended and Restated Non-Employee Director Compensation Policy each non-employee director is eligible to receive compensation for his or her service consisting of annual cash retainers, each paid in four equal quarterly installments and equity awards. Each director receives an annual base cash retainer of $35,000 for such service. The non-executive chairperson of our board of directors receives an additional annual base cash retainer of $27,500 for such service.

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 and each of the other members of the audit committee receives an annual cash retainer of $7,500.

•The chairperson of our compensation committee receives an annual cash retainer of $12,000 for such service and each of the other members of the compensation committee receives an annual cash retainer of $6,000.

•The chairperson of our nominating and corporate governance committee receives an annual cash retainer of $8,000 for such service and each of the other members of the nominating and corporate governance committee receives an annual cash retainer of $4,000.

•Directors may elect to receive share options or restricted share units, or a mixture of both in lieu of his/her cash retainer on the date on which such retainer would otherwise have been paid in cash on the terms and subject to the conditions set forth below with respect to director equity awards, provided that any such election is made no later than December 31 of the calendar year prior to the year that the compensation is earned; and provided further that each such share option and restricted share unit award will vest in full upon the first anniversary of the vesting commencement date, with the vesting commencement date being the first day of each calendar quarter for which such cash retainer is earned, or the date of election to the board in the case of a newly appointed director.

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 $110,000.

•The equity awards will be granted as a mix of share options and restricted share units, at such director's discretion. Each director must determine their mix of equity awards no later than 30 days prior to the applicable grant date.

•All equity awards will vest on the one-year anniversary of the grant date.

•The value of a share option to be granted under this policy will be determined using the same method we use to calculate the grant-date fair value of share options in our financial statements, except that no provision will be made for estimated forfeitures related to service-based vesting. The actual number of shares to be granted under a restricted share unit award under this policy will be determined by dividing the grant date value by a 30-day volume weighted average trading price (ending on the trading day immediately preceding the grant date).

We also reimburse our non-employee directors for reasonable travel and other expenses incurred in connection with attending our board of director and committee meetings.

In May 2023 the board of directors resolved to suspend annual equity awards due to be granted to non-employee directors pursuant to our Amended and Restated Non-Employee Director Compensation Policy and any further grants of awards pursuant to that policy to be made in lieu of cash compensation. In lieu of the annual equity award to be made at the 2023 and 2024 annual general meetings of shareholders, a cash amount of $40,000 to the non-employee directors was paid.

Clawback Policy

In October 2023, our Board adopted a written Compensation Recovery Policy (the Clawback Policy) addressing the recovery of incentive-based compensation from current or former covered officers to ensure compliance with the requirements of Nasdaq Listing Rule 5608, which implements Rule 10D-1 under the Exchange Act. If the Company is required to prepare an accounting restatement due to the material noncompliance of the Company with any financial reporting requirement under the federal securities laws, the Company will recover any erroneously awarded incentive-based compensation from current or former officers subject to reporting under Section 16 of the Exchange Act that was received within the applicable recovery period. The Compensation Committee of the Board has the discretion to make all decisions under this policy. The Company did not have an accounting restatement in 2024.

Anti-Hedging and Anti-Pledging Policies

We prohibit our directors, officers, and employees from engaging in the following transactions with respect to securities of the Company:

•short sales;

•transactions in put or call options;

•hedging transactions;

•margin accounts;

•pledges; or

•other inherently speculative transactions.

Policies and Practices Related to the Grant of Equity Awards

We grant equity awards, including incentive share options (ISOs), nonstatutory share options (NSOs) and restricted share units (RSUs), among other forms of awards, to our employees from time to time as part of an individual employee's compensation or for retention purposes. We may also grant equity awards to individuals upon hire. Our Amended and Restated Non-Employee Director Compensation Policy provides for the grant of an annual equity award to directors at our annual general meeting of shareholders.

During the last fiscal year, neither the board of directors nor the compensation committee approved the grant of any equity awards to employees or consultants. In May 2023 the board of directors resolved to suspend annual equity awards due to be granted to non-employee directors pursuant to our Amended and Restated Non-Employee Director Compensation Policy including any grants which would be otherwise made at the annual general meeting of shareholders in 2024.

Risk Considerations in Our Compensation Program

Our compensation committee has reviewed and evaluated the philosophy and standards on which our compensation plans have been developed and implemented across our Company. It is our belief that our compensation programs do not encourage inappropriate actions or risk taking by our executive officers. We do not believe that any risks arising from our employee compensation policies and practices are reasonably likely to have a material adverse effect on our Company. In addition, we do not believe that the mix and design of the components of our executive compensation program encourage management to assume excessive risks.

Securities Authorized for Issuance Under Equity Compensation Plans

As of December 31, 2024, we had two equity compensation plans, the 2018 Equity Incentive Plan (2018 Plan), and the 2015 Equity Incentive Plan (2015 Plan), each of which were approved by our shareholders. In addition, from time to time, the compensation committee grants inducement equity awards to individuals as an inducement material to the individual's entry into employment with us within the meaning of Nasdaq Listing Rules, pursuant to our 2021 Inducement Equity Incentive Plan (2021 Inducement Plan) that was adopted by our board of directors without shareholder approval. See "Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters - Equity Compensation Plan Information" to see the table which provides certain aggregate information with respect to all of our equity compensation plans in effect as of December 31, 2024.

2021 Inducement Equity Incentive Plan (2021 Inducement Plan)

On November 24, 2021, our board of directors adopted without shareholder approval the 2021 Inducement Plan and, subject to the adjustment provisions of the 2021 Inducement Plan, reserved 333,333 ordinary shares for issuance pursuant to equity awards granted under the 2021 Inducement Plan. In accordance with Nasdaq Listing Rule 5635(c)(4), awards under the 2021 Inducement Plan may only be made to individuals who were not previously employees or nonemployee directors of the Company (or following such individuals' bona fide period of non-employment with the Company), as an inducement material to the individuals' entry into employment with the Company. The 2021 Inducement Plan provides for the grant of NSOs, share appreciation rights (SARs), restricted shares, RSUs, performance-based share awards, and other share awards.

As of December 31, 2024, share options to purchase 4,833 ordinary shares were outstanding under our 2021 Inducement Plan, with a weighted-average exercise price of $2.08 per share. No other forms of awards were outstanding under the 2021 Inducement Plan as of December 31, 2024.

2018 Equity Incentive Plan (2018 Plan)

Our board of directors adopted our 2018 Plan in March 2018 and our shareholders approved the 2018 Plan in May 2018, and the Plan was most recently amended and restated in June 2020 and further amended in June 2021. Our 2018 Plan authorizes the award of incentive share options that may qualify for favorable tax treatment under U.S. tax laws to their recipients under Section 422 of the Code, or ISOs, NSOs, SARs, restricted shares, RSUs, performance-based share awards, and other share awards, which are collectively referred to as awards. We may grant awards under the 2018 Plan to our employees, including our officers, and employees of our affiliates. A separate sub-plan to the 2018 Plan has been established for the purpose of granting awards to our non-employee directors and consultants and non-employee directors and consultants of our affiliates, which we refer to as the Sub-Plan. The provisions of the 2018

Plan apply in their entirety to any awards made under the Sub-Plan save for certain amendments set out in the Sub-Plan required in the context of awards to our non-employee directors and consultants and non-employee directors and consultants of our affiliates, rather than employees, including references to eligible participants under the Sub-Plan.

As of December 31, 2024, share options to purchase 829,574 ordinary shares were outstanding under our 2018 Plan, with a weighted-average exercise price of $1.95 per share.

Our 2018 Plan is administered by our board of directors or a duly authorized committee or subcommittee of our board of directors. Our board of directors has authorized our compensation committee to administer certain aspects of the 2018 Plan. For purposes of this summary, where appropriate in the relevant context, the term "board of directors" may include the compensation committee or any other committee to whom the board of directors delegates authority, as indicated in the 2018 Plan. Our board of directors may also delegate to one or more of our officers the authority to designate employees (other than officers) to receive specified awards under the 2018 Plan and determine the number of shares subject to such awards.

Our board of directors has the authority to construe and interpret our 2018 Plan, grant and amend awards, determine the terms of such awards and make all other determinations necessary or advisable for the administration of the plan, including, but not limited to, repricing share options or SARs without prior shareholder approval. All determinations, interpretations and constructions made by the board of directors in good faith will not be subject to review by any person and will be final, binding and conclusive on all persons.

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.

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 the surviving or acquiring corporation (or its parent company);
- arrange for the assignment of any reacquisition or repurchase rights held by us in respect of ordinary shares issued under an award to a surviving or acquiring corporation (or its parent company);
- accelerate the vesting, in whole or in part, of the award and, if applicable, the time at which the award may be exercised, and provide for its termination prior to the transaction if it is not exercised at or prior to the closing of the transaction;
- arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us with respect to the award;
- 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 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 vested 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 at least 50% of our outstanding securities, (iii) the consummation of a merger or consolidation where we do not survive the transaction or (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 (the 2014 Act) or (z) Chapter 2 of Part 9 of the 2014 Act.

The board of directors need not take the same action or actions with respect to all awards or portions of awards or with respect to all participants. The board of directors may take different actions with respect to the vested and unvested portions of an award.

Notwithstanding the foregoing, 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" (as defined below), if a participant's services to the Company (or its successor in the change in control) are involuntarily terminated without "cause" (as defined below) or a participant resigns service to the Company (or its successor in the change in control) in all capacities for "good reason" (as defined below), and, in either case other than as a result of the participant's death or disability, then as of the date of the participant's termination of service, the vesting and exercisability of any then-unvested award held by a participant will be accelerated in full.

A "change in control" for purposes of the 2018 Plan is defined, in summary, as (i) the acquisition by a person or a group of more than 50% of our outstanding shares other than by virtue of a merger or consolidation; (ii) our involvement in a merger, consolidation,

or similar transaction, unless our shareholders prior to such event continue to own, in substantially the same proportions as before the transaction, more than 50% of the entity surviving such event; our shareholders or our board approves a plan of liquidation or dissolution or our complete dissolution or liquidation otherwise occurs; (iii) a sale or other disposition of all or substantially all of our assets (other than a sale to an entity more than 50% of which is owned by our shareholders in substantially the same proportions as their ownership of us immediately prior to such transaction); or (iv) a change, without approval by our board of directors, of a majority of our board of directors. In addition, any one or more of the above events may be effected pursuant to (x) a compromise or arrangement sanctioned by the Irish courts under Section 450 of the 2014 Act, (y) a scheme, contract or offer which has become binding on all shareholders pursuant to Section 609 of the 2014 Act, or (z) a bid pursuant to Regulation 23 or 24 of the European Communities (Takeover Bids (Directive 2004/25/EC)) Regulations 2006.

"Cause" as used in the 2018 Plan has the meaning ascribed to such term in any written agreement between the participant and us defining such term but, in the absence of such a definition, means, in summary (i) the participant's commission of a felony or crime involving fraud, dishonesty or moral turpitude; (ii) the participant's attempted commission of, or participation in, a fraud or act of dishonesty against us or an affiliate of ours; (iii) the participant's intentional, material violation of any contract or agreement between the participant and us or an affiliate of ours, of any statutory duty owed to us or an affiliate of ours; (iv) the participant's unauthorized use or disclosure of our (or an affiliate's) confidential information or trade secrets; or (v) the participant's gross misconduct. In addition, "good reason" as used in the 2018 Plan has the meaning ascribed to such term in any written agreement between the participant and us defining such term but, in the absence of such a definition, means, in summary, any of the following actions taken without the participant's consent: (i) a material reduction of the participant's base compensation, other than a reduction that applies generally to all executive officers; (ii) a material reduction in the participant's authority, duties and responsibilities; (iii) failure or refusal of a successor of ours to materially assume our obligations under the participant's offer letter and/or employment agreement, if applicable, in the event of a change in control; or (iv) a 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 addition, in order to resign for "good reason" a participant must provide written notice of the event giving rise to "good reason" to us within 90 days after the condition arises, allow us at least 30 days to cure such provision, and if we fail to cure the condition, resign from all positions not later than 90 days after the end of such cure period.

Our board of directors has the authority to amend, suspend, or terminate our 2018 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our shareholders. No awards may be granted under our 2018 Plan while it is suspended or after it is terminated.

2015 Equity Incentive Plan (2015 Plan)

Our board of directors adopted, and our shareholders approved our 2015 Plan in November 2015. The 2015 Plan was amended most recently in May 2017. The 2015 Plan provided for the grant of ISOs, NSOs, restricted share awards, RSUs, SARs, and other share awards to our employees, directors and consultants.

Since the 2018 Plan became effective, we no longer grant awards under the 2015 Plan. However, any outstanding awards granted under the 2015 Plan remain outstanding, subject to the terms of the 2015 Plan and the applicable award agreements, until such outstanding share options are exercised or until they terminate or expire by their terms.

•*Authorized Shares*. As of December 31, 2024, share options to purchase 7,313 ordinary shares were outstanding under our 2015 Plan, with a weighted-average exercise price of $49.70 per share. No other forms of awards were outstanding under the 2015 Plan as of December 31, 2024.

•*Plan Administration*. Our 2015 Plan may be administered by our board of directors or another duly authorized committee. Our 2015 Plan is currently administered by our compensation committee. Our board of directors or another duly authorized committee has the authority to construe and interpret our 2015 Plan, amend the plan and outstanding awards and make all other determinations necessary or advisable for the administration of the plan, including, but not limited to, repricing share options or SARs without prior shareholder approval.

•*Corporate Transactions*. Our 2015 Plan provides that in the event of a corporate transaction, each outstanding award will be treated as determined by our board of directors unless otherwise provided in an award agreement or other written agreement between us and the award holder. The board of directors may generally take the same actions as summarized above in connection with awards under the 2018 Plan, and the definition of a corporate transaction under the 2015 Plan is substantially the same as such defined term in the 2018 Plan.

•*Transferability*. Awards granted under our 2015 Plan may not be transferred in any manner other than by will or by the laws of descent and distribution or as otherwise determined by our compensation committee or under the terms of our 2015 Plan or an applicable award agreement.

•*Plan Amendment or Termination.* Our board of directors or another duly authorized committee has the authority to amend, suspend, or terminate our 2015 Plan, provided that such action does not materially impair the existing rights of any

participant without such participant's written consent. Certain material amendments also require the approval of our shareholders.

Health and Welfare Benefits

All of our named executive officers are eligible to participate in our employee benefit plans, including our medical, dental, and vision insurance plans, in each case on the same basis as all of our other full-time employees.

***401(k)* Plan**

We maintain a defined contribution retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees may defer eligible compensation on a pre-tax basis, up to the statutorily prescribed annual limits on contributions under the Code. 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. The Company historically made discretionary contributions to the 401(k) Plan for the benefit of certain employees excluding executive officers.

Limitation on Liability and Indemnification of Directors and Officers

Our Articles of Association, and indemnification agreements with our board of directors and executive officers provide for indemnification for our directors and officers.

Rule 10b5-1 Sales Plans

Our directors and officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell ordinary shares on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer generally may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may generally buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information, subject to compliance with the terms of our insider trading policy.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters.

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of January 31, 2025 by:

(a)each person, or group of affiliated persons, known by us to beneficially own more than 5% of our ordinary shares;

(b)each of our named executive officers;

(c)each of our directors; and

(d)all of our executive officers and directors as a group.

Beneficial ownership is determined according to the rules of the SEC and generally means that a person has beneficial ownership of a security if he, she, or it possesses sole or shared voting or investment power of that security, including share options that are exercisable within 60 days of January 31, 2025, restricted share units that vest within 60 days of January 31, 2025 and shares issuable upon exercise of warrants within 60 days of January 31, 2025. Our ordinary shares issuable pursuant to share options, restricted share units and warrants are deemed outstanding for computing the percentage of the person holding such share options, restricted share units or warrants and the percentage of any group of which the person is a member, but are not deemed outstanding for computing the percentage of any other person. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons named in the table below have sole voting and investment power with respect to all ordinary shares shown that they beneficially own, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Section 13(d) and 13(g) of the Securities Act of 1933, as amended. Percentage ownership is based on 33,781,845 ordinary shares outstanding on January 31, 2025. Except as otherwise set forth below, the address of the beneficial owner is c/o Iterum Therapeutics plc, 3 Dublin Landings, North Wall Quay, Dublin 1, Ireland.

	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
Directors and Named Executive Officers:		
Corey N. Fishman[(1)]	448,625	1.1 %
Judith M. Matthews[(2)]	75,577	*
Sailaja Puttagunta	10,369	*
Michael Dunne, MD[(3)]	382,448	1.1 %
Beth P. Hecht	18,839	*
Ronald M. Hunt[(4)]	775,152	2.3 %
David G. Kelly[(5)]	54,323	*
All current executive officers and directors as a group (6 persons)[(6)])	1,754,964	5.0 %

*less than 1%

(1) Consists of (a) 137,062 shares beneficially owned by Mr. Fishman, and (b) 123,919 shares issuable to Mr. Fishman pursuant to warrants exercisable within 60 days of January 31, 2025; and (c) 187,644 shares issuable to Mr. Fishman pursuant to share options exercisable within 60 days of January 31, 2025.

(2) Consists of (a) 8,135 shares beneficially owned by Ms. Matthews, and (b) 67,442 shares issuable to Ms. Matthews pursuant to share options exercisable within 60 days of January 31, 2025.

(3) Consists of (a) 220,001 shares beneficially owned by Dr. Dunne, and (b) 162,447 shares issuable to Dr. Dunne pursuant to warrants exercisable within 60 days of January 31, 2025.

(4) Consists of (a) 14,346 shares beneficially owned by Mr. Hunt, (b) 43,886 shares issuable to Mr. Hunt pursuant to share options exercisable within 60 days of January 31, 2025; and (c) (i) 253,898 shares reported as beneficially owned by New Leaf Venture III, L.P. (NLV-III), New Leaf Venture Associates III, L.P. (NLVA-III LP) and New Leaf Venture Management III, L.L.C. (NLVM-III LLC), of which each such entity reports sole voting power with respect to 253,898, shared voting power with respect to zero shares, sole dispositive power with respect to 253,898 shares and shared dispositive power with respect to zero shares, (ii) 91,122 shares held by New Leaf Biopharma Opportunities II, L.P. (NBPO-II), New Leaf BPO Associates II, L.P. (NBPO-IIA) and New Leaf BPO Management II, L.L.C. (NBPO-IIM), of which each such entity reports sole voting power with respect to 91,122 shares, shared voting power with respect to zero shares, sole dispositive power with respect to 91,122 shares and shared dispositive power with respect to zero shares, and (iii) 273,679 shares issuable to NLV-III and 98,221 shares issuable to NBPO-II pursuant to warrants exercisable within 60 days of January 31, 2025. NLVA-III LP is the general partner of NLV-III and NLVM-III LLC is the general partner of NLVA-III LP. NBPO-IIA is the general partner of NBPO-II and NBPO-IIM is the general partner of NBPO-IIA. Mr. Hunt, a member of our board of directors, and Vijay K. Lathi are individual managers of NLVM-III LLC and individual managers of NPBO-IIM, and as a result may be deemed to have shared power to vote and dispose of these shares. The address for each of the reporting persons other than Vijay K. Lathi is c/o New Leaf Venture Partners, 420 Lexington Avenue, Suite 408, New York, NY 10170. The address for Vijay K. Lathi is c/o New Leaf Venture Partners, 2730 Sand Hill Road, Suite 110, Menlo Park, CA 94025. We obtained certain of the information regarding beneficial ownership of these shares from Schedule 13D/A that was filed with the SEC on February 21, 2021.

(5) Consists of (a) 2,473 shares beneficially owned by Mr. Kelly and (b) 51,850 shares issuable to Mr. Kelly pursuant to share options exercisable within 60 days of January 31, 2025.

(6) Includes (a) 745,876 shares held by the current directors and executive officers and their affiliates, (b) 350,822 shares issuable to the current directors and executive officers pursuant to share options exercisable within 60 days of January 31, 2025, and (c) 658,266 shares issuable to the current directors and their affiliates pursuant to warrants exercisable within 60 days of January 31, 2025.

Equity Compensation Plan Information

The following table provides certain aggregate information with respect to all of our equity compensation plans in effect as of December 31, 2024. As of December 31, 2024, we had two equity compensation plans, the 2018 Plan, and the 2015 Plan, each of which were approved by our shareholders. In addition, from time to time, the compensation committee grants inducement equity awards to individuals as an inducement material to the individual's entry into employment with us within the meaning of Nasdaq Listing Rules, pursuant to our 2021 Inducement Plan that was adopted by our board of directors without shareholder approval.

Plan category	(a) Number of securities to be issued upon exercise of outstanding options	(b) Weighted average exercise price of outstanding options	(c) Number of securities remaining for future issuance under equity compensation plan (excluding securities reflected in column (a))(3)
Equity compensation plans approved by shareholders	836,887	$ 2.37	192,890
Equity compensation plans not approved by shareholders	4,833 (1)	2.08	314,766
Total	841,720	2.37	507,656

(1) Represents share option awards granted as an inducement material to the acceptance of employment with the Company by certain newly hired employees in accordance with Nasdaq Listing Rule 5635(c)(4) under our 2021 Inducement Plan.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The following is a description of transactions since January 1, 2023, to which we have been a party, in which the amount involved exceeds $120,000, and in which any of our directors, executive officers or holders of more than 5% of our share capital, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest. We refer to such transactions as "related party transactions" and such persons as "related parties." With the approval of our board of directors, we engaged in the related party transactions described below. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, from unaffiliated third parties.

Participation in Rights Offering

On August 9, 2024, we completed a rights offering (the 2024 Rights Offering) in which holders validly subscribed for 6,121,965 units (Units) at a subscription price of $1.21 per whole Unit, consisting of (a) one ordinary share, (b) a warrant to purchase 0.50 ordinary shares, at an exercise price of $1.21 per whole ordinary share from the date of issuance through its expiration one year from the date of issuance (1-year warrants) and (c) a warrant to purchase one ordinary share, at an exercise price of $1.21 per whole ordinary share from the date of issuance through its expiration five years from the date of issuance (the 5-year warrants and, together with the 1-year warrants, the warrants). Certain of our directors and affiliates of our directors participated in the 2024 Rights Offering. The table below sets forth the aggregate number of Units purchased by our directors or an affiliate of a director, in connection with the 2024 Rights Offering:

Name	Units	Aggregate Purchase Price ($)
Corey N. Fishman	82,613	99,961.73
Michael W. Dunne	106,247	128,558.87
New Leaf Ventures III, L.P.	182,453	220,768.13
New Leaf Biopharma Opportunities II, L.P.	65,481	79,232.01
Total	436,794	528,520.74

2020 Investor Rights Agreement

In January 2020 we entered into an investor rights agreement (the "2020 Investor Rights Agreement") by and among, Iterum Therapeutics Bermuda Limited ("Iterum Bermuda"), us, ITIL, Iterum Therapeutics US Limited and Iterum Therapeutics US Holding

Limited, as guarantors (the "Guarantors") and a limited number of accredited investors (the "Private Placement Investors") (including certain of our directors and holders of more than 5% of our share capital, or an affiliate or immediate family member thereof) pursuant to which Iterum Bermuda and the Guarantors agreed to file a registration statement covering (a) in the case of a registration statement on Form S-1, the resale of 6.500% Exchangeable Senior Subordinated Notes due 2025, fully and unconditionally guaranteed on an unsecured senior subordinated basis by the Guarantors, in the original principal amount of $1,000.00 (the "Exchangeable Notes"), the ordinary shares issuable in connection with the exchange of the Exchangeable Notes (the "Exchange Shares") and the Limited Recourse Royalty-Linked Subordinated Notes, fully and unconditionally guaranteed on an unsecured senior subordinated basis by the Guarantors (the "Royalty-Linked Notes") or (b) in the case of a registration statement on Form S-3, the Exchange Shares (the securities in (a) and (b) together, the "Registrable Securities"). Under the 2020 Investor Rights Agreement, we agreed to file an initial registration statement covering the resale by the Private Placement Investors of their Registrable Securities, which registration statement on Form S-1 was filed in September 2020 and declared effective on October 6, 2020. If the registration statement covering the Registrable Securities ceases to be effective for resales of Registrable Securities for more than 60 consecutive days or for more than 120 days in any 12-month period, then, subject to the terms of the 2020 Investor Rights Agreement, additional interest will accrue on the Exchangeable Notes and the Royalty-Linked Notes. On January 31, 2025, the Exchangeable Notes matured and Iterum Bermuda repaid to the holders thereof an aggregate principal amount of $11.1 million together with accrued interest of $3.6 million.

2017 Investor Rights Agreement

In May 2017, we entered into an amended and restated investor rights agreement with holders of our preferred shares and ordinary shares, including certain holders of more than 5% of our share capital, our executive officers, certain of our directors, and entities affiliated with certain of our directors (the "2017 Investor Rights Agreement"). Since the closing of our initial public offering, those holders are entitled to certain registration rights, including the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. The 2017 Investor Rights Agreement also gave the shareholders that are parties thereto the right to participate in new issuances of equity securities by us, subject to certain exceptions. This right to participate in new issuances of equity securities terminated by its terms upon the completion of our initial public offering in May 2018.

Arrangements with Executive Officers and Directors

For a description of the compensation arrangements that we have with our executive officers and directors, see "Executive Officer and Director Compensation - Employment Agreements with Executive Officers" and "Executive Officer and Director Compensation - Non-Employee Director Compensation Policy."

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. In addition, our subsidiary, Iterum Therapeutics US Limited, has entered into an indemnification agreement with each of our directors and executive officers. These agreements, among other things, require us to indemnify an indemnitee to the fullest extent permitted by applicable law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the indemnitee in any action or proceeding, including any action or proceeding by us or in our right, arising out of the person's services as a director or executive officer. We also maintain a directors and officers liability insurance policy which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

Consulting Agreement - Michael W. Dunne, M.D.

Michael W. Dunne, M.D. served as our Chief Scientific Officer until he resigned in December 2020. Following Dr. Dunne's resignation in December 2020, in February 2021, our subsidiary, ITIL, entered into a consulting agreement with Dr. Dunne for the provision of general support and strategic advice in connection with the NDA (the 2021 Consulting Agreement). The commencement date for the purposes of the provision of the services pursuant to the 2021 Consulting Agreement was December 22, 2020, and the term was to end on September 30, 2021, unless extended by mutual agreement of the parties or terminated in accordance with the terms of the 2021 Consulting Agreement. Either party could terminate the 2021 Consulting Agreement with two months' notice in writing to the other party. ITIL was to pay Dr. Dunne $16,900 per month pursuant to the 2021 Consulting Agreement and Dr. Dunne was also entitled to payments in an aggregate amount of up to $220,000 on the achievement of milestones set out in the 2021 Consulting Agreement, for so long as he continued to provide services thereunder on the occurrence of such milestones. The 2021 Consulting Agreement was amended, effective September 30, 2021, to extend the term of the 2021 Consulting Agreement by three months, or until December 31, 2021. It was further amended, effective as of December 31, 2021, to extend the term by an additional three months, or until March 31, 2022, and to reduce the monthly service fee payable thereunder to $10,000 per month. The 2021 Consulting Agreement terminated on March 31, 2022. On May 25, 2022, ITIL entered into the Dunne Consulting Agreement, effective May 1, 2022, for the provision of general support and strategic advice in connection with the potential resubmission of the NDA including the design and conduct of a Phase 3 clinical trial to support such resubmission. The Dunne Consulting Agreement entitles Dr. Dunne to consulting fees of $5,000 per month. The Dunne Consulting Agreement was amended, effective December 31, 2022, to extend the term of the Dunne Consulting Agreement by six months, or until June 30, 2023. It was further amended on June 15, 2023 to extend the term by six months, or until

December 31, 2023, on December 27, 2023 to extend the term until June 30, 2024, on August 9, 2024, with an effective date of June 30, 2024, to extend the term until December 31, 2024 and on December 5, 2024 extend the term until June 30, 2025. An aggregate of $60,000 was expensed for services provided by Dr. Dunne in 2024 pursuant to the Dunne Consulting Agreement, as amended. As of February 5, 2025, an aggregate of $5,000 was expensed for services provided by Dr. Dunne to date in 2025 pursuant to the Dunne Consulting Agreement.

Consulting Agreement - Sailaja Puttagunta, M.D.

For a description of the consulting arrangement that we have with Dr. Puttagunta, see "Executive Compensation - Narrative Disclosure to Executive Officer Summary Compensation Table." As of February 5, 2025, an aggregate of $10,400 was expensed for services provided by Dr. Puttagunta to date in 2025 pursuant to the Puttagunta Consulting Agreement.

Related Party Transaction Policy

We have adopted a formal written policy that our executive officers, directors, key employees, holders of more than 5% of any class of our voting securities, and any member of the immediate family of and any entity affiliated with any of the foregoing persons, are not permitted to enter into a related-party transaction with us without the prior consent of our audit committee, or other independent body of our board of directors in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest. Any request for us to enter into a transaction with an executive officer, director, principal shareholder, or any of their immediate family members or affiliates, in which the amount involved exceeds $120,000, is required to first be presented to our audit committee for review, consideration, and approval. In approving or rejecting any such proposal, our audit committee will consider the relevant facts and circumstances available and deemed relevant to our audit committee, including, but not limited to, whether the transaction will be on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related party's interest in the transaction.

Some of the transactions described in this section were entered into prior to the adoption of this policy. Although we did not have a written policy for the review and approval of transactions with related persons prior to May 2018, our board of directors has historically reviewed and approved any transaction where a director or officer had a financial interest, including the relevant transactions described above. Prior to approving such a transaction, the material facts as to a director's or officer's relationship or interest in the agreement or transaction were disclosed to our board of directors. Our board of directors took this information into account when evaluating the transaction and in determining whether such transaction was fair to us and in the best interest of all our shareholders.

Board Determination of Independence

Applicable rules of The Nasdaq Stock Market, or Nasdaq, require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq rules require that within one year of the date of the completion of an initial public offering, all the members of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

In order to be considered independent for purposes of Rule 10A-3 under the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

In order to be considered independent for purposes of Rule 10C-1 under the Exchange Act, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including any consulting, advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In April 2024, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that none of Ms. Hecht, Mr. Hunt, Mr. Kelly, representing three of our five current directors, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under Rule 5605(a)(2) of the Nasdaq Listing Rules. Mr. Fishman is not an independent director under Rule 5605(a)(2) because he is our President and Chief Executive Officer. Dr. Dunne is not an independent director under Rule 5605(a)(2) as he has received compensation from the Company in excess of $120,000 during a period of twelve consecutive months within the three years preceding the determination of independence. Our board of directors has also determined that Messrs. Kelly and Hunt and Ms. Hecht, who comprise our audit committee, Mr. Hunt and Ms. Hecht, who comprise our compensation committee, and Messrs. Hunt and Kelly, who comprise our nominating and corporate governance committee, satisfy the independence standards for such committees established by the SEC

and Nasdaq. In making such determination, our board of directors considered the relationships that each such non-employee director has with our Company, including the transactions described below in "Certain Relationships and Related Party Transactions", and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our shares by each non-employee director as described above in "Share Ownership of Certain Beneficial Owners and Management".

Item 14. Principal Accounting Fees and Services.

The following table presents fees for professional audit services and other services rendered by KPMG to us for the fiscal years ended December 31, 2024 and 2023:

	December 31, 2024	December 31, 2023
Audit fees (1)	$ 297,610	$ 258,000
Audit related fees (2)	—	—
Tax fees (3)	65,934	64,762
All other fees	—	—
	$ 363,544	$ 322,762

(1) "Audit Fees" consist of fees for professional services performed by KPMG for the audit of our annual financial statements, the review of interim financial statements, and related services that are normally provided in connection with registration statements on Form S-3.
(2) "Audit-related fees" consist of fees billed by an independent registered public accounting firm for assurance and related services that are reasonably related to the performance of the audit or review of our consolidated financial statements.
(3) "Tax fees" consist of fees for professional services, including tax consulting and compliance performed by KPMG in Ireland and the US.

All of these services were pre-approved by the audit committee in accordance with the "*Policy on Audit Committee Pre-Approval of Services*" described below. No work carried out in connection with the audit of our financial statements was performed by persons other than KPMG's full time, permanent employees.

Policy on Audit Committee Pre-Approval of Services

Consistent with SEC policies regarding auditor independence, the audit committee has responsibility for appointing, setting compensation and overseeing the work of our independent registered public accounting firm. In recognition of this responsibility, the audit committee reviews and pre-approves all audit and permissible non-audit services provided by our independent registered public accounting firm; provided, however, that de minimis non-audit services may instead be approved in accordance with applicable SEC rules.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(1)Consolidated Financial Statements

See Index to Consolidated Financial Statements at Item 8 herein.

(2)Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the consolidated financial statements or notes thereto.

(3)Exhibits

The following is a list of exhibits filed or furnished as part of this Annual Report on Form 10-K;

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
3.1	Amended and Restated Constitution of Iterum Therapeutics plc		Form 8-K (Exhibit 3.1)	May 04, 2023	001-38503
3.2	Memorandum of Association of Iterum Therapeutics Bermuda Limited		Form S-1 (Exhibit 3.2)	March 20, 2020	333-237326
3.3	Bye-Laws of Iterum Therapeutics Bermuda Limited		Form S-1 (Exhibit 3.3)	March 20, 2020	333-237326
3.4	Constitution of Iterum Therapeutics International Limited		Form 10-K (Exhibit 3.4)	March 12, 2021	001-38503
3.5	Amended and Restated Certificate of Incorporation of Iterum Therapeutics US Limited		Form 10-K (Exhibit 3.5)	March 12, 2021	001-38503
3.6	Bylaws of Iterum Therapeutics US Limited		Form 10-K (Exhibit 3.6)	March 12, 2021	001-38503
3.7	Certificate of Amendment of Certificate of Incorporation of Iterum Therapeutics US Holding Limited		Form 10-K (Exhibit 3.7)	March 12, 2021	001-38503
3.8	Bylaws of Iterum Therapeutics US Holding Limited		Form 10-K (Exhibit 3.8)	March 12, 2021	001-38503
4.1	Form of Ordinary Share Certificate of Registrant.		Form S-1 (Exhibit 4.1)	May 1, 2018	333-224582
4.2	Indenture (including form of note), dated January 21, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and U.S. Bank National Association, as trustee.		Form 10-K (Exhibit 4.2)	March 12, 2020	001-38503
4.3	Form of 6.500% Exchangeable Senior Subordinated Note due 2025 (included within Exhibit 4.2).		Form 10-K (Exhibit 4.3)	March 12, 2020	001-38503
4.4	Indenture (including form of note), dated January 21, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited, Iterum Holders' Representative LLC and Computershare Trust Company, N.A., as trustee.		Form 10-K (Exhibit 4.4)	March 12, 2020	001-38503
4.5	Form of Limited Recourse Royalty-Linked Subordinated Note (included within Exhibit 4.4).		Form 10-K (Exhibit 4.5)	March 12, 2020	001-38503
4.6	Form of Warrant to Subscribe for Ordinary Shares issued to purchasers in connection with Securities Purchase Agreement dated June 3, 2020		Form 8-K (Exhibit 4.1)	June 04, 2020	001-38503

4.7	Form of Placement Agent Warrant to Subscribe for Ordinary Shares issued to designees of H.C. Wainwright & Co., LLC in connection with Securities Purchase Agreement dated June 3, 2020		Form 8-K (Exhibit 4.2)	June 04, 2020	001-38503
4.8	Form of Warrant to Subscribe for Ordinary Shares issued to purchasers in connection with Securities Purchase Agreement dated June 30, 2020		Form 8-K (Exhibit 4.1)	July 01, 2020	001-38503
4.9	Form of Placement Agent Warrant to Subscribe for Ordinary Shares issued to designees of H.C. Wainwright & Co., LLC in connection with Securities Purchase Agreement dated June 30, 2020		Form 8-K (Exhibit 4.2)	July 01, 2020	001-38503
4.10	Form of Ordinary Share Purchase Warrant to Subscribe for Ordinary Shares issued to purchasers in connection with the Securities Purchase Agreement dated October 22, 2020		Form 8-K (Exhibit 4.1)	October 27, 2020	001-38503
4.11	Form of Pre-Funded Ordinary Share Purchase Warrant to Subscribe for Ordinary Shares issued to purchasers in connection with the Securities Purchase Agreement dated October 22, 2020		Form 8-K (Exhibit 4.2)	October 27, 2020	001-38503
4.12	Form of Placement Agent Ordinary Share Purchase Warrant to Subscribe for Ordinary Shares issued to designees of H.C. Wainwright & Co., LLC in connection with the Placement Agent Agreement dated October 22, 2020		Form 8-K (Exhibit 4.3)	October 27, 2020	001-38503
4.13	Form of Underwriter Warrant to subscribe for ordinary shares issued to designees of H.C. Wainwright & Co., LLC in connection with the Amended and Restated Underwriting Agreement dated February 3, 2021		Form 8-K (Exhibit 4.1)	February 5, 2021	001-38503
4.14	Form of Placement Agent Warrant to Subscribe for Ordinary Shares issued to designees of H.C. Wainwright & Co., LLC in connection with Securities Purchase Agreement dated February 9, 2021		Form 8-K (Exhibit 4.1)	February 11, 2021	001-38503
4.15	Form of 1-Year Warrant to Subscribe for Ordinary Shares		Form S1/A (Exhibit 4.15)	July 17, 2024	333-280045
4.16	Form of 5-Year Warrant to Subscribe for Ordinary Shares		Form S1/A (Exhibit 4.16)	July 17, 2024	333-280045
4.17	Form of 1-Year Warrant Agent Agreement, by and between Iterum Therapeutics plc and Computershare Trust Company, N.A.		Form S1/A (Exhibit 4.17)	July 17, 2024	333-280045
4.18	Form of 5-Year Warrant Agent Agreement, by and between Iterum Therapeutics plc and Computershare Trust Company, N.A.		Form S1/A (Exhibit 4.18)	July 17, 2024	333-280045
4.19	Form of Rights Certificate		Form S1/A (Exhibit 4.19)	July 17, 2024	333-280045
4.20	Description of Registrant's Securities	X			
10.1†	License Agreement by and among Registrant, Iterum Therapeutics International Limited and Pfizer Inc. dated as of November 18, 2015.		Form S-1 (Exhibit 10.1)	May 1, 2018	333-224582
10.2	Amended and Restated Investor Rights Agreement by and between Registrant and certain of its shareholders dated May 18, 2017.		Form S-1 (Exhibit 10.2)	May 1, 2018	333-224582
10.3	2015 Equity Incentive Plan, as amended		Form 10-Q (Exhibit 10.1)	November 10, 2022	001-38503
10.4	Forms of U.S. Stock Option Agreement, Stock Option Grant Notice and Notice of Exercise under the 2015 Equity Incentive Plan.		Form S-1 (Exhibit 10.4)	May 1, 2018	333-224582
10.5	Forms of Irish Stock Option Agreement, Stock Option Grant Notice and Notice of Exercise under the 2015 Equity Incentive Plan.		Form S-1 (Exhibit 10.5)	May 1, 2018	333-224582

10.6	Amended and Restated 2018 Equity Incentive Plan, as amended		Form 10-Q (Exhibit 10.2)	November 10, 2022	001-38503
10.7	Forms of U.S. Stock Option Terms and Conditions and Stock Option Grant Notice under the 2018 Equity Incentive Plan.		Form S-1 (Exhibit 10.7)	May 1, 2018	333-224582
10.8	Forms of International Stock Option Terms and Conditions and Stock Option Grant Notice under the 2018 Equity Incentive Plan.		Form S-1 (Exhibit 10.8)	May 1, 2018	333-224582
10.9	Form of Restricted Share Unit Award Agreement under the 2018 Equity Incentive Plan.		Form S-1 (Exhibit 10.9)	May 1, 2018	333-224582
10.10	Form of 2020 Restricted Share Unit Award Agreement under the 2018 Equity Incentive Plan.		Form 10-K (Exhibit 10.10)	March 12, 2020	001-38503
10.11	Form of Indemnity Agreement by and between the Registrant and its directors and officers.		Form S-1 (Exhibit 10.10)	May 1, 2018	333-224582
10.12	Form of Indemnity Agreement by and between Iterum Therapeutics US Limited and its directors and officers.		Form S-1 (Exhibit 10.11)	May 1, 2018	333-224582
10.13+	Employment Terms by and between Iterum Therapeutics US Limited and Corey N. Fishman dated November 18, 2015.		Form S-1 (Exhibit 10.12)	May 1, 2018	333-224582
10.14+	Amendment to Employment Agreement by and between Iterum Therapeutics US Limited and Corey N. Fishman dated May 2, 2018.		Form S-1/A (Exhibit 10.13)	May 4, 2018	333-224582
10.15+	Employment Terms by and between Iterum Therapeutics US Limited and Judith M. Matthews dated November 18, 2015.		Form S-1 (Exhibit 10.15)	May 1, 2018	333-224582
10.16+	Amendment to Employment Agreement by and between Iterum Therapeutics US Limited and Judith M. Matthews dated May 2, 2018.		Form S-1/A (Exhibit 10.16)	May 4, 2018	333-224582
10.17+	Consulting Agreement dated May 25, 2022 between Iterum Therapeutics International Limited and Dr. Michael Dunne		Form 10-Q (Exhibit 10.1)	August 12, 2022	001-38503
10. 18	Amendment to Consulting Agreement dated December 31, 2022 between Iterum Therapeutics International Limited and Dr. Michael Dunne		Form 10-K (Exhibit 10.18)	March 16, 2023	001-38503
10.19	Amendment to Consulting Agreement dated June 15, 2022 between Iterum Therapeutics International Limited and Dr. Michael Dunne		Form 10-Q (Exhibit 10.1)	August 11, 2023	001-38503
10.20	Amendment to Consulting Agreement dated December 27, 2023 between Iterum Therapeutics International Limited and Dr. Michael Dunne		Form 10-K (Exhibit 10.20)	March 28, 2024	001-38503
10.21	Amendment to Consulting Agreement dated August 9, 2023 between Iterum Therapeutics International Limited and Dr. Michael Dunne		Form 10-Q (Exhibit 10.1)	November 14, 2024	001-38503
10.22	Amendment to Consulting Agreement dated December 5, 2024 between Iterum Therapeutics International Limited and Dr. Michael Dunne	X			
10.23+	Share Award Letter dated February 17, 2021 issued by Iterum Therapeutics plc to Dr. Michael Dunne and accepted by Dr. Michael Dunne on February 21, 2021		Form 10-Q (Exhibit 10.2)	May 14, 2021	001-38503
10.24+	Employment Terms by and between Iterum Therapeutics US Limited and Dr. Sailaja Puttagunta dated October 27, 2021		Form 10-K (Exhibit 10.19)	March 28, 2022	001-38503

10.25	Consulting Agreement dated May 29, 2024 between Iterum Therapeutics International Limited and Dr. Sailaja Puttagunta	Form 10-Q (Exhibit 10.1)	August 14, 2024	001-38503
10.26+	Amended and Restated Non-Employee Director Compensation Policy	Form 8-K (Exhibit 10.1)	March 16, 2021	001-38503
10.27	Warrant to Subscribe for Shares, issued to Silicon Valley Bank, dated April 27, 2018.	Form S-1/A (Exhibit 10.21)	May 4, 2018	333-224582
10.28	Warrant to Subscribe for Shares, issued to Life Sciences Fund II LLC, dated April 27, 2018.	Form S-1/A (Exhibit 10.22)	May 4, 2018	333-224582
10.29	Securities Purchase Agreement, dated as of January 16, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and the Investors party thereto.	Form 8-K (Exhibit 10.1)	January 17, 2020	001-38503
10.30	Investor Rights Agreement, dated January 21, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and the Investors party thereto.	Form 10-K (Exhibit 10.26)	March 12, 2020	001-38503
10.31	Securities Purchase Agreement, dated as of June 3, 2020, by and among Iterum Therapeutics plc and the purchasers party thereto	Form 10-Q (Exhibit 10.1)	August 6, 2020	001-38503
10.32	Securities Purchase Agreement, dated as of June 30, 2020, by and among Iterum Therapeutics plc and the purchasers party thereto	Form 10-Q (Exhibit 10.2)	August 6, 2020	001-38503
10.33	Securities Purchase Agreement, dated as of October 22, 2020, by and among Iterum Therapeutics plc and the purchasers party thereto	Form 10-Q (Exhibit 10.1)	November 16, 2020	001-38503
10.34	Securities Purchase Agreement, dated as of February 9, 2021, by and among Iterum Therapeutics plc and the purchasers party thereto	Form 10-K (Exhibit 10.28)	March 12, 2021	001-38503
10.35	Iterum Therapeutics plc 2021 Inducement Equity Incentive Plan, as amended	Form 10-Q (Exhibit 10.3)	November 10, 2022	001-38503
10.36	Form of US Nonstatutory Share Option Terms and Conditions and Nonstatutory Share Option Grant Notice under the 2021 Inducement Equity Incentive Plan	Form S-8 (Exhibit 99.2)	December 9, 2021	333-261558
10.37	Form of International Nonstatutory Share Option Terms and Conditions and Nonstatutory Share Option Grant Notice under the 2021 Inducement Equity Incentive Plan	Form S-8 (Exhibit 99.3)	December 9, 2021	333-261558
10.38	Form of Restricted Share Unit Award Agreement under the 2021 Inducement Equity Incentive Plan	Form S-8 (Exhibit 99.4)	December 9, 2021	333-261558
10.39	At the Market Offering Agreement, dated October 7, 2022 by and between Iterum Therapeutics plc and H.C. Wainwright & Co., LLC	Form S-3 (Exhibit 1.2)	October 7, 2022	333-267795
10.40	Share Option Cancellation Agreement, dated July 7, 2022, between Iterum Therapeutics plc and Corey N. Fishman	Form 10-Q (Exhibit 10.2)	August 12, 2022	001-38503
10.41	Share Option Cancellation Agreement, dated July 7, 2022, between Iterum Therapeutics plc and Judith M. Matthews	Form 10-Q (Exhibit 10.3)	August 12, 2022	001-38503
10.42	Promissory Note dated October 28, 2024 from Iterum Therapeutics International Limited to Pfizer Inc.	Form 8-K (Exhibit 10.1)	November 1, 2024	001-38503

19.1	Insider Trading and Trading Window Policy		Form 10-K (Exhibit 19)	March 28, 2024	001-38503
21.1	Subsidiaries of the Registrant		Form 10-K (Exhibit 21.1)	March 12, 2020	001-38503
22.1	Subsidiary Guarantors and Subsidiary Issuers		Form 10-K (Exhibit 22.1)	March 12, 2021	001-38503
23.1	Consent of KPMG, Independent Registered Public Accounting Firm	X			
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			
97.1	Policy for the Recovery of Erroneously Awarded Compensation, effective October 2, 2023		Form 10-K (Exhibit 91.1)	March 28, 2024	001-38503
101.INS	Inline XBRL Instance Document	X			
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents	X			
104	Cover Page Interactive Data File (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101)	X			

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+ Indicates management contract or compensatory plan.

† Confidential treatment has been granted for certain provisions omitted from this Exhibit pursuant to Rule 406 promulgated under the Securities Act. The omitted information has been filed separately with the Securities and Exchange Commission.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

ITERUM THERAPEUTICS PLC

Date: February 7, 2025

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

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ Corey N. Fishman Corey N. Fishman	President and Chief Executive Officer (Principal Executive Officer)	February 7, 2025
/s/ Judith M. Matthews Judith M. Matthews	Chief Financial Officer (Principal Financial and Accounting Officer)	February 7, 2025
/s/ Michael Dunne Michael Dunne M.D.	Director	February 7, 2025
/s/ Ronald M. Hunt Ronald M. Hunt	Director	February 7, 2025
/s/ David G. Kelly David G. Kelly	Director	February 7, 2025
/s/ Beth Hecht Beth Hecht	Director	February 7, 2025

Exhibit 4.20

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

Iterum Therapeutics plc ("we", "us" or the "Company") has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"): our Ordinary Shares, $0.01 par value per share.

DESCRIPTION OF SHARE CAPITAL

The following description of our share capital is intended as a summary only and therefore is not a complete description of our share capital. This description is based upon, and is qualified by reference to, our Memorandum and Articles of Association (our "Constitution"), and applicable provisions of the Irish Companies Act 2014 (the "Irish Companies Act"). You should read our Constitution including our Articles of Association, which are filed as an exhibit to the Annual Report on Form 10-K of which this exhibit is a part, for the provisions that are important to you.

Capital Structure—Authorized Share Capital

Our authorized share capital consists of 80,000,000 ordinary shares of $0.01 each and 100,000,000 undesignated preferred shares of $0.01 each.

We may issue shares subject to the maximum authorized share capital contained in our Constitution. The authorized share capital may be increased or reduced (but not below the number of issued ordinary shares or preferred shares, as applicable) by a resolution approved by a simple majority of the votes of our shareholders cast at a general meeting (referred to under Irish law as an "ordinary resolution") (unless otherwise determined by the directors). The shares comprising our authorized share capital may be divided into shares of any nominal value.

The rights and restrictions to which the ordinary shares are subject are prescribed in our Articles of Association. Our Articles of Association entitle our board of directors, without shareholder approval, to determine the terms of our preferred shares. Preferred shares may be preferred as to dividends, rights upon liquidation or voting in such manner as our board of directors may resolve. The preferred shares may also be redeemable at the option of the holder of the preferred shares or at our option and may be convertible into or exchangeable for shares of any of our other class or classes, depending on the terms of such preferred shares.

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

Whenever an alteration or reorganization of our share capital would result in any of our shareholders becoming entitled to fractions of a share, our board of directors may, on behalf of those shareholders that would become entitled to fractions of a share, arrange for the sale of the shares representing fractions and the distribution of the net proceeds of sale in due proportion among the shareholders who would have been entitled to the fractions.

Issuance of Shares

As a matter of Irish law, the board of directors of a company may issue authorized but unissued new shares without shareholder approval once authorized to do so by the Articles of Association of the company or by an ordinary resolution adopted by the shareholders at a general meeting. The authority conferred may be granted for a maximum period of five years, at which point it must be renewed by the shareholders by an ordinary resolution. Our board of directors is authorized pursuant to a shareholder resolution passed on May 3, 2023 to issue new ordinary or preferred shares up to the amount of the authorized but unissued share capital at that date without shareholder approval up to May 3, 2028.

Pre-emption Rights, Share Warrants and Share Options

Under Irish law certain statutory pre-emption rights apply automatically in favor of shareholders where shares, warrants, convertible instruments or options are to be issued for cash. However, we have opted out of these pre-emption rights by way of shareholder resolution passed on October 8, 2024 as permitted under Irish company law.Irish law requires this opt-out to be renewed every five years by a resolution approved by not less than 75% of the votes of our shareholders cast at a general meeting (referred to under Irish law as a "special resolution") and our current opt-out will expire on May 3, 2028. If the opt-out is not renewed, shares issued for cash must be offered to our existing shareholders on a *pro rata* basis to their existing shareholding before the shares can be issued to any new shareholders. The statutory pre-emption rights do not apply where shares are issued for non-cash consideration (such as in a share-for-share acquisition) and do not apply to the issue of non-equity shares (that is, shares that have the right to participate only up to a specified amount in any income or capital distribution) or where shares are issued pursuant to an employee share option or similar equity plan.

Our Articles of Association provide that, subject to any shareholder approval requirement under any laws, regulations or the rules of any stock exchange to which we are subject, the board of directors is authorized, from time to time, in its discretion, to grant such persons, for such periods and upon such terms as the board of directors deems advisable, options to purchase such number of shares of any class or classes or of any series of any class as the board of directors may deem advisable, and to cause warrants or other appropriate instruments evidencing such options to be issued. The Irish Companies Act provides that directors may issue share warrants or options without shareholder approval once authorized to do so by the Articles of Association. We are subject to the rules of the Nasdaq Capital Market that require shareholder approval of certain equity plans and share issuances. Our board of directors may authorize the issuance of shares upon exercise of warrants or options without shareholder approval or authorization (up to the relevant authorized share capital limit).

Under Irish law, we are prohibited from allotting shares without consideration. Accordingly, at least the nominal value of the shares issued underlying any restricted share award, restricted share unit, performance share award, bonus share or any other share-based grant must be paid pursuant to the Irish Companies Act.

Dividends

Under Irish law, dividends and distributions may only be made from distributable reserves. Distributable reserves, broadly, means the accumulated realized profits of a company, so far as not previously utilized by distribution or capitalization, less accumulated realized losses of a company, so far as not previously written off in a reduction or reorganization of capital, and includes reserves created by way of capital reduction, on a standalone basis. In addition, no distribution or dividend may be made unless our net assets are equal to, or in excess of, the aggregate of our called-up share capital plus undistributable reserves and the distribution does not reduce our net assets below such aggregate. Undistributable reserves include the undenominated capital, the amount by which our accumulated unrealized profits, so far as not previously utilized by any capitalization, exceed our accumulated unrealized losses, so far as not previously written off in a reduction or reorganization of capital and any other reserve that we are prohibited from distributing by applicable law.

The determination as to whether or not we have sufficient distributable reserves to fund a dividend must be made by reference to the "relevant financial statements" of the Company. The "relevant financial statements" are either the last set of unconsolidated annual audited financial statements or unaudited financial statements properly prepared in accordance with the Irish Companies Act, which give a "true and fair view" of the Company's unconsolidated financial position in accordance with accepted accounting practice in Ireland. The "relevant financial statements" must be filed in the Companies Registration Office (the official public registry for companies in Ireland) prior to the making of the distribution.

Consistent with Irish law, our Articles of Association authorize the directors to declare interim dividends without shareholder approval out of funds lawfully available for the purpose, to the extent they appear justified by profits and subject always to the requirement to have distributable reserves at least equal to the amount of the proposed dividend. The board of directors may also recommend a dividend to be approved and declared by our shareholders at

a general meeting. The board of directors may direct that the payment be made by distribution of assets, shares or cash and no dividend declared or paid may exceed the amount recommended by the directors. Dividends may be paid in U.S. dollars or any other currency.

Our directors may deduct from any dividend payable to any shareholder any amounts payable by such shareholder to us in relation to our shares.

Our directors may also authorize the issuance of shares with preferred rights to participate in our declared dividends. The holders of preferred shares may, depending on their terms, rank senior to our ordinary shares in terms of dividend rights and/or be entitled to claim arrears of a declared dividend out of subsequently declared dividends in priority to ordinary shareholders.

Share Repurchases, Redemptions and Conversions

Overview

Our Articles of Association provide that, in general, any ordinary share which we have agreed to acquire shall be deemed to be a redeemable share. Accordingly, for Irish company law purposes, the repurchase of ordinary shares by us may technically be effected as a redemption of those shares as described below under "—Repurchases and Redemptions." If our Articles of Association did not contain such provisions, all repurchases by us would be subject to many of the same rules that apply to purchases of our shares by subsidiaries described below under "—Purchases by Subsidiaries" including the shareholder approval requirements described below. Except where otherwise noted, when we refer to repurchasing or buying back our ordinary shares, we are referring to the redemption of ordinary shares by us pursuant to the Articles of Association or the purchase of our ordinary shares by a subsidiary of the Company, in each case in accordance with our Articles of Association and Irish law as described below. Holders of our ordinary shares have no right to convert the shares into any other security.

Repurchases and Redemptions

Under Irish law, a company may issue redeemable shares and redeem them out of distributable reserves (which are described above under "Dividends") or, if the company proposes to cancel the shares on redemption, the proceeds of a new issue of shares for that purpose. The redemption of redeemable shares may only be made by us where the nominal value of the issued share capital that is not redeemable is not less than 10% of the nominal value of the total issued share capital of the company. All redeemable shares must also be fully paid and the terms of redemption of the shares must provide for payment on redemption. Redeemable shares may, upon redemption, be cancelled or held in treasury. Based on the provisions of our articles described above, shareholder approval will not be required to redeem our shares.

We may also be given an additional general authority by our shareholders to purchase our own shares on-market, which would take effect on the same terms and be subject to the same conditions as applicable to purchases by our subsidiaries as described below.

Our board of directors may also issue preferred shares or other classes or series of shares which may be redeemed at either our option or the option of the shareholder, depending on the terms of such preferred shares. Please see "—Capital Structure—Authorized Share Capital."

Repurchased and redeemed shares may be cancelled or held as treasury shares. The nominal value of treasury shares held by us at any time must not exceed 10% of the nominal value of our issued share capital. We may not exercise any voting rights in respect of any shares held as treasury shares. Treasury shares may be cancelled by us or re-issued subject to certain conditions.

Purchases by Subsidiaries

Under Irish law, an Irish or non-Irish subsidiary of the Company may purchase our shares either as overseas market purchases on a recognized stock exchange such as the Nasdaq or off-market. For a subsidiary of ours to make market purchases of our shares, our shareholders must provide general authorization for such purchase by way of ordinary resolution. However, as long as this general authority has been granted, no specific shareholder authority for a particular market purchase by a subsidiary of our shares is required. We may elect to seek such general authority, which must expire no later than 18 months after the date on which it was granted, at our annual general meetings.

For an off-market purchase by a subsidiary of ours, the proposed purchase contract must be authorized by special resolution of the shareholders before the contract is entered into. The person whose shares are to be bought back cannot vote in favor of the special resolution and from the date of the notice of the meeting at which the resolution approving the contract is proposed, the purchase contract must be on display or must be available for inspection by shareholders at our registered office from the date of the notice of the meeting at which the resolution approving the contract is to be proposed.

In order for a subsidiary of ours to make an on-market purchase of our shares, such shares must be purchased on a "recognized stock exchange." The Nasdaq Capital Market, on which our ordinary shares are listed, is specified as a recognized stock exchange for this purpose by Irish company law.

The number of shares held by our subsidiaries at any time will count as treasury shares and will be included in any calculation of the permitted treasury share threshold of 10% of the nominal value of our issued share capital. While a subsidiary holds shares of ours, it cannot exercise any voting rights in respect of those shares. The acquisition of our shares by a subsidiary of ours must be funded out of distributable reserves of the subsidiary.

Lien on Shares, Calls on Shares and Forfeiture of Shares

Our Articles of Association provide that we will have a first and paramount lien on every share for all debts and liabilities of any shareholder to the Company, whether presently due or not, payable in respect of such share. Subject to the terms of their allotment, directors may call for any unpaid amounts in respect of any shares to be paid, and if payment is not made within 14 days after notice demanding payment, we may sell the shares. These provisions are standard inclusions in the Articles of Association of an Irish company limited by shares and will only be applicable to our shares that have not been fully paid up. See "—Transfer and Registration of Shares."

Consolidation and Division; Subdivision

Under our Articles of Association, we may, by ordinary resolution (unless the directors determine otherwise), divide all or any of our issued share capital into shares of smaller nominal value than our existing shares (often referred to as a share split) or consolidate all or any of our issued share capital into shares of larger nominal value than is fixed by our memorandum of association (often referred to as a reverse share split), provided that the proportion between the amount paid for such share and the amount, if any, unpaid on each reduced share after the subdivision remains the same.

Reduction of Share Capital

We may, by ordinary resolution (unless the directors determine otherwise), reduce our authorized but unissued share capital in any way. We also may, by special resolution and subject to confirmation by the Irish High Court, reduce or cancel our issued share capital in any manner permitted by the Irish Companies Act.

Annual General Meetings of Shareholders

We are required to hold an annual general meeting within 18 months of incorporation and at intervals of no more than 15 months thereafter, provided that an annual general meeting is held in each calendar year following the first annual general meeting and no more than nine months after our fiscal year-end. Any annual general meeting may be held outside Ireland, provided that technological means are provided to enable shareholders to participate in the meeting without leaving Ireland.

Notice of an annual general meeting must be given to all of our shareholders and to our auditors. Our Articles of Association provide for a minimum notice period of 21 clear days (i.e. 21 days excluding the day when the notice is given or deemed to be given and the day of the event for which it is given or on which it is to take effect), which is the minimum permitted under Irish law.

The only matters which must, as a matter of Irish company law, be transacted at an annual general meeting are (i) the consideration of the statutory financial statements, report of the directors, 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 in advance of the meeting to be considered thereat.

Extraordinary General Meetings of Shareholders

Our extraordinary general meetings may be convened by (i) the board of directors, (ii) on requisition of the shareholders holding not less than 10% of our paid-up share capital carrying voting rights, (iii) in certain circumstances, on requisition of our auditors; or (iv) in exceptional cases, by order of the Irish High Court.

Extraordinary general meetings are generally held for the purpose of approving shareholder resolutions as may be required from time to time. At any extraordinary general meeting, only such business will be conducted as is set forth in the notice thereof or is proposed pursuant to and in accordance with the procedures and requirements set out in our Articles of Association.

Notice of an extraordinary general meeting must be given to all of our shareholders and to our auditors. Under Irish law and our Articles of Association, the minimum notice periods are 21 clear days' notice in writing for an extraordinary general meeting to approve a special resolution and 14 clear days' notice in writing for any other extraordinary general meeting.

In the case of an extraordinary general meeting convened by our shareholders, the proposed purpose of the meeting must be set out in the requisition notice. Upon receipt of any such valid requisition notice, our board of directors has 21 days to convene a meeting of our shareholders to vote on the matters set out in the requisition notice. This meeting must be held within two months of the receipt of the requisition notice. If the board of directors does not convene the meeting within such 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 our receipt of the requisition notice.

If the board of directors becomes aware that our net assets are not greater than half of the amount of our called-up share capital, our directors must convene an extraordinary general meeting of our shareholders not later than 28 days from the date that the fact is known to a director to be held not later than 56 days from such date. This meeting must be convened for the purposes of considering whether any, and if so what, measures should be taken to address the situation.

Quorum for General Meetings

Our Articles of Association provide that no business shall be transacted at any general meeting unless a quorum is present. One or more members whose name is entered in the register of members of the Company as a registered holder of shares present in person or by proxy at any meeting of shareholders holding not less than a majority of the issued shares that carry the right to vote at the meeting constitutes a quorum for the conduct of any business at a general meeting.

Voting

Our Articles of Association provide that all votes at a general meeting will be decided on a poll and that the board of directors or the chairman may determine the manner in which the poll is to be taken and the manner in which the votes are to be counted.

Every shareholder is entitled to one vote for each ordinary share that he or she holds as of the record date for the meeting. Voting rights may be exercised by shareholders registered in our share register as of the record date for the meeting or by a duly appointed proxy, which proxy need not be a shareholder. Where interests in shares are held by a nominee trust company, this company may exercise the rights of the beneficial holders on their behalf as their proxy. All proxies must be appointed in the manner prescribed by our Articles of Association, which provide that our board of directors may permit shareholders to notify us of their proxy appointments electronically.

In accordance with our Articles of Association, our directors may from time to time authorize the issuance of preferred shares or any other class or series of shares. These shares may have such voting rights as may be specified in the terms of such shares (e.g., they may carry more votes per share than ordinary shares or may entitle their holders to a class vote on such matters as may be satisfied in the terms of such shares). Treasury shares or shares of ours that are held by our subsidiaries will not be entitled to be voted at general meetings of shareholders.

Irish company law requires special resolutions of the shareholders at a general meeting to approve certain matters.

Examples of matters requiring special resolutions include:

- amending the objects as contained in our memorandum of association;
- amending our Articles of Association;
- approving a change of name;
- authorizing the entering into of a guarantee or provision of security in connection with a loan, quasi-loan or credit; transaction to a director or connected person;
- opting out of pre-emption rights on the issuance of new shares;
- re-registration from a public limited company to a private company;
- purchase of own shares off-market;
- reduction of issued share capital;
- sanctioning a compromise/scheme of arrangement;
- resolving that the company be wound up by the Irish courts;
- resolving in favor of a shareholders' voluntary winding-up;
- re-designation of shares into different share classes;

- setting the re-issue price of treasury shares; and
- variation of class rights attaching to classes of shares (where our Articles of Association do not provide otherwise).

Neither Irish law nor any of our constituent documents places limitations on the right of non-resident or foreign owners to vote or hold our shares.

Variation of Rights Attaching to a Class or Series of Shares

Under our Articles of Association and the Irish Companies Act, any variation of class rights attaching to our issued shares must be approved by an ordinary resolution passed at a general meeting of the shareholders of the affected class or with the consent in writing of the holders of a majority of the issued shares of that class of shares entitled to vote on such variation. The rights conferred upon the holder of any pre-existing issued shares shall not be deemed to be varied by the issuance of any preferred shares.

The provisions of our Articles of Association relating to general meetings apply to general meetings of the holders of any class of shares except that the necessary quorum is determined in reference to the shares of the holders of the class. Accordingly, for general meetings of holders of a particular class of shares, a quorum consists of one or more shareholders present in person or by proxy holding not less than a majority of the issued and outstanding shares of the class entitled to vote at the meeting in question.

Record Date

Our Articles of Association provide that the board of directors may fix in advance a date as the record date (i) for any such determination of members entitled to notice of or to vote at a general meeting of the members, which record date shall not be more than 60 days before the date of such meeting, and (ii) for the purpose of determining the members entitled to receive payment of any dividend or other distribution, or in order to make a determination of members for any other proper purpose, which record date shall not be more than 60 days prior to the date of payment of such dividend or other distribution or the taking of any action to which such determination of members is relevant.

If no record date is fixed for the determination of members entitled to notice of or to vote at a meeting of members, the date immediately preceding the date on which notice of the meeting is deemed given under our Articles of Association will be the record date for such determination of members.

Shareholder Proposals

Under Irish law, there is no general right for a shareholder to put items on the agenda of an annual general meeting of a U.S.-listed company, other than as set out in the Articles of Association of a company. Under our Articles of Association, in addition to any other applicable requirements, for business or nominations to be properly brought before an annual general meeting by a shareholder, such shareholder must have given timely notice thereof in proper written form to our corporate secretary.

To be timely for an annual general meeting, a shareholder's notice to our secretary as to the business or nominations to be brought before the meeting must be delivered to or mailed and received at our registered office (i) with respect to our first annual general meeting as a public limited company, not later than the 10th day following the day on which public announcement of the date of such annual general meeting is made and (ii) with respect to all other annual general meetings not less than 90 days nor more than 120 days before the first anniversary of the notice convening our annual general meeting for the prior year. In the event that the date of the annual general meeting is changed by more than 30 days from the first anniversary date of the preceding year's annual general meeting, notice by the member must be so delivered by close of business on the day that is not earlier than 120 days prior to such annual general meeting and not later than the close of business on the later of (a) 90 days prior to the day of the contemplated annual general meeting or (b) 10 days after the day on which public announcement of the date of the contemplated annual general meeting is first made by us. In no event shall the public announcement of an adjournment

or postponement of an annual general meeting commence a new time period (or extend any time period) for the giving of a shareholder's notice.

To be timely for business or nominations of a director at an extraordinary general meeting, notice must be delivered, or mailed and received not less than 90 days nor more than 120 days prior to the date of such extraordinary general meeting or, if the first public announcement of the date of the extraordinary general meeting is less than 100 days prior to the date of the meeting, by close of business 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 U.S. Securities and Exchange Commission rules regarding the solicitation of proxies for the election of directors pursuant to Regulation 14A under the Exchange Act. For other business that a shareholder proposes to bring before the meeting, the notice must include a brief description of the business, the reasons for proposing the business at the meeting and a discussion of any material interest of the shareholder in the business. Whether the notice relates to a nomination to the board of directors or to other business to be proposed at the meeting, the notice also must include information about the shareholder and the shareholder's holdings of our shares. The chairman of the meeting shall have the power and duty to determine whether any business proposed to be brought before the meeting was made or proposed in accordance with these procedures (as set out in our Articles of Association), and if any proposed business is not in compliance with these provisions, to declare that such defective proposal shall be disregarded.

Shareholders' Suits

In Ireland, the decision to institute proceedings on behalf of a company is generally taken by the company's board of directors. In certain limited circumstances, a shareholder may be entitled to bring a derivative action on our behalf. The central question at issue in deciding whether a minority shareholder may be permitted to bring a derivative action is whether, unless the action is brought, a wrong committed against us would otherwise go unredressed. The cause of action may be against a director, another person or both.

A shareholder may also bring proceedings against us in his or her own name where the shareholder's rights as such have been infringed or where our affairs are being conducted, or the powers of the board of directors are being exercised, in a manner oppressive to any shareholder or shareholders or in disregard of their interests as shareholders. Oppression connotes conduct that is burdensome, harsh or wrong. This is an Irish statutory remedy under Section 212 of the Irish Companies Act and the court can grant any order it sees fit, including providing for the purchase or transfer of the shares of any shareholder.

Inspection of Books and Records

Under Irish law, shareholders have the right to: (i) receive a copy of our Constitution; (ii) inspect and obtain copies of the minutes of general meetings and any resolutions; (iii) inspect and receive a copy of the register of shareholders, register of directors and secretaries, register of directors' interests and other statutory registers maintained by us; (iv) inspect copies of directors' service contracts; (v) inspect copies of instruments creating charges; (vi) receive copies of statutory financial statements and directors' and auditors' reports which have previously been sent to shareholders prior to an annual general meeting; and (vii) receive financial statements of a subsidiary company of ours which have previously been sent to shareholders prior to an annual general meeting for the preceding 10 years. Our auditors will also have the right to inspect all of our books, records and vouchers. The auditors' report must be circulated to the shareholders with our financial statements prepared in accordance with Irish law with the notice of annual general meeting and must be presented to our shareholders at our annual general meeting.

Acquisitions

There are a number of mechanisms for acquiring an Irish public limited 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% in value of the shares of such participating class or series held by the shareholders voting on the scheme of arrangement, in each case at the relevant meeting or meetings. A scheme of arrangement, if authorized by the shareholder of each participating class or series and the court, is binding on all of the shareholders of each participating class or series;

- through a tender or takeover offer by a third party, in accordance with the Irish Takeover Rules and the Irish Companies Act, for all of our shares. Where the holders of 80% or more of our shares (excluding any shares already beneficially owned by the bidder) have accepted an offer for their shares, the remaining shareholders may also be statutorily required to transfer their shares, unless, within one month, the non-tendering shareholders can obtain an Irish court order otherwise providing. If the offeror has acquired acceptances of 80% of all of our shares but does not exercise its "squeeze-out" right, then the non-accepting shareholders also have a statutory right to require the bidder to acquire their shares on the same terms as the original offer, or such other terms as the bidder and the non-tendering shareholders may agree or on such term as an Irish court, on application of the bidder or non-tendering shareholder, may order. If our shares were to be listed on the Euronext Dublin or another regulated stock exchange in the European Union, the aforementioned 80% threshold would be increased to 90%;

- by way of a transaction with a company incorporated in the European Economic Area which includes all member states of the European Union and Norway, Iceland and Liechtenstein ("EEA") under the European Union (Cross-Border Conversions, Mergers and Divisions) Regulations 2023. Such a transaction must be approved by a special resolution and by the Irish High Court. If we are being merged with another EEA company under the EU Cross-Border Mergers Directive (EU) 2019/2121 and the consideration payable to our shareholders is not all in the form of cash, our shareholders may be entitled to require their shares to be acquired at fair value; and

- by way of a merger with another Irish company under the Irish Companies Act which must be approved by a special resolution and by the Irish High Court.

Appraisal Rights

Generally, under Irish law, shareholders of an Irish company do not have statutory appraisal rights. If we are being merged as the transferor company with another EEA company under the European Union (Cross-Border Conversions, Merger and Divisions) Regulations 2023 or if we are being merged with another Irish company under the Irish Companies Act, (i) any of our shareholders who voted against the special resolution approving the merger or (ii) if 90% of our shares are held by the successor company, any other of our shareholders, may be entitled to require that the successor company acquire its shares for cash.

Disclosure of Interests in Shares

Under the Irish Companies Act, there is a notification requirement for shareholders who acquire or cease to be interested in 3% of the shares of an Irish public limited company. Our shareholders must therefore make such a notification to us if, as a result of a transaction, the shareholder will become interested in 3% or more of our shares or if, as a result of a transaction, a shareholder who was interested in 3% or more of our shares ceases to be so interested. Where a shareholder is interested in 3% or more of our shares, the shareholder must notify us of any alteration of his or her interest that brings his or her total holding through the nearest whole percentage number, whether an increase or a reduction. The relevant percentage figure is calculated by reference to the aggregate nominal value of the shares in which the shareholder is interested as a proportion of the entire nominal value of our issued share capital (or any such class of share capital in issue). Where the percentage level of the shareholder's interest does not amount to a whole percentage, this figure may be rounded down to the next whole number. All such disclosures should be notified to us within five business days of the transaction or alteration of the shareholder's interests that gave rise to the notification requirement. If a shareholder fails to comply with these notification requirements, the shareholder's rights

in respect of any of our shares it holds will not be enforceable, either directly or indirectly. However, such person may apply to the court to have the rights attaching to such shares reinstated.

In addition to these disclosure requirements, under the Irish Companies Act, we may by notice in writing, require a person whom we know or have reasonable cause to believe to be, or at any time during the three years immediately preceding the date on which such notice is issued to have been, interested in shares comprised in our relevant share capital to: (i) indicate whether or not it is the case and (ii) where such person holds or has during that time held an interest in our ordinary shares, to provide additional information, including the person's own past or present interests in our shares. If the recipient of the notice fails to respond within the reasonable time period specified in the notice, we may apply to court for an order directing that the affected shares be subject to certain restrictions, as prescribed by the Irish Companies Act, as follows:

- any transfer of those shares, or in the case of unissued shares any transfer of the right to be issued with shares and any issue of shares, will be void;
- no voting rights will be exercisable in respect of those shares;
- no further shares will be issued in right of those shares or in pursuance of any offer made to the holder of those shares; and
- no payment will be made of any sums due from us on those shares, whether in respect of capital or otherwise.

Where our shares are subject to these restrictions, the court may order the shares to be sold and may also direct that the shares shall cease to be subject to these restrictions.

In the event we are in an offer period pursuant to the Irish Takeover Rules, accelerated disclosure provisions apply for persons holding an interest in our securities of 1.0% or more.

Irish Takeover Rules

A transaction in which a third party seeks to acquire 30% or more of our voting rights will be governed by the Irish Takeover Panel Act 1997 and the Irish Takeover Rules made thereunder and will be regulated by the Irish Takeover Panel. The "General Principles" of the Irish Takeover Rules and certain important aspects of the Irish Takeover Rules are described below. Takeovers by means of a scheme of arrangement are also generally subject to these regulations.

General Principles

The Irish Takeover Rules are built on the following General Principles, which will apply to any transaction regulated by the Irish Takeover Panel:

- in the event of an offer, all holders of securities of the target company should be afforded equivalent treatment and, if a person acquires control of a company, the other holders of securities must be protected;
- the holders of the securities in the target company must have sufficient time and information to enable them to reach a properly informed decision on the offer;
- where it advises the holders of securities, the board of the target company must give its views on the effects of implementation of the offer on employment, conditions of employment and the locations of the target company's places of business;
- the board of the target company must act in the interests of the company as a whole and must not deny the holders of securities the opportunity to decide on the merits of the offer;

- false markets must not be created in the securities of the target company, the bidder or of any other company concerned by the offer in such a way that the rise or fall of the prices of the securities becomes artificial and the normal functioning of the markets is distorted;

- a bidder must announce an offer only after ensuring that he or she can fulfil in full, any cash consideration, if such is offered, and after taking all reasonable measures to secure the implementation of any other type of consideration;

- a target company must not be hindered in the conduct of its affairs for longer than is reasonable by an offer for its securities; and
- a substantial acquisition of securities (whether such acquisition is to be effected by one transaction or a series of transactions) shall take place only at an acceptable speed and shall be subject to adequate and timely disclosure.

Mandatory Bid

Under certain circumstances, a person who acquires shares or other of our voting rights may be required under the Irish Takeover Rules to make a mandatory cash offer for our remaining outstanding shares at a price not less than the highest price paid for the shares by the acquirer (or any parties acting in concert with the acquirer) during the previous 12 months. This mandatory bid requirement is triggered if an acquisition of shares would (i) increase the aggregate holding of an acquirer (including the holdings of any parties acting in concert with the acquirer) to shares representing 30% or more of our voting rights, or (ii) in the case of a person holding (together with its concert parties) shares representing 30% or more of our voting rights, after giving effect to the acquisition, increase the percentage of the voting rights held by that person (together with its concert parties) by 0.05% within a 12-month period. Any person (excluding any parties acting in concert with the holder) holding shares representing more than 50% of the voting rights of a company is not subject to these mandatory offer requirements in purchasing additional securities.

Voluntary Bid; Requirements to Make a Cash Offer and Minimum Price Requirements

A voluntary offer is an offer that is not a mandatory offer. If a person makes a voluntary offer to acquire outstanding ordinary shares of ours, the offer price must be no less than the highest price paid for our shares by the bidder or its concert parties during the three-month period prior to the commencement of the offer period. The Irish Takeover Panel has the power to extend the "look back" period to 12 months if the Irish Takeover Panel, taking into account the General Principles, believes it is appropriate to do so.

If the bidder or any party acting in concert with it has acquired our ordinary shares (i) during the period of 12 months prior to the commencement of the offer period which represent more than 10% of our total ordinary shares or (ii) at any time after the commencement of the offer period, the offer must be in cash (or accompanied by a full cash alternative) and the price per ordinary share must not be less than the highest price paid by the bidder or any party acting in concert with it during, in the case of (i), the 12-month period prior to the commencement of the offer period and, in the case of (ii), the offer period. The Irish Takeover Panel may apply this rule to a bidder who, together with any party acting in concert with it, has acquired less than 10% of our total ordinary shares in the 12-month period prior to the commencement of the offer period if the Irish Takeover Panel, taking into account the General Principles, considers it just and proper to do so.

An offer period will generally commence from the date of the first announcement of the offer or proposed offer.

Substantial Acquisition Rules

The Irish Takeover Rules also contain rules governing substantial acquisitions of shares which restrict the speed at which a person may increase his or her holding of shares and rights over shares to an aggregate of between 15% and 30% of the voting rights in our shares. Except in certain circumstances, an acquisition or series of acquisitions of shares or rights over shares representing 10% or more of the voting rights in our shares 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 the voting rights in our shares and such acquisitions are made within a period of seven days. These rules also require accelerated disclosure of certain other acquisitions of shares or rights over shares relating to such holdings.

Anti-Takeover Provisions

Shareholder Rights Plan

Our Articles of Association expressly authorize our board of directors to adopt a shareholder rights plan, subject to applicable law.

Frustrating Action

Under the Irish Takeover Rules, our board of directors is not permitted to take any action which might frustrate an offer for our shares once our board of directors has received an approach which may lead to an offer or has reason to believe an offer is imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of shares, options or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any time during which the board of directors has reason to believe an offer is imminent. Exceptions to this prohibition are available where:

- the action is approved by our shareholders at a general meeting; or
- the Irish Takeover Panel has given its consent, where:
  - it is satisfied the action would not constitute frustrating action;
  - our shareholders that hold 50% of the voting rights state in writing that they approve the proposed action and would vote in favor of it at a general meeting;
  - the action is taken in accordance with a contract entered into prior to the announcement of the offer; or
  - the decision to take such action was made before the announcement of the offer and either has been at least partially implemented or is in the ordinary course of business.

Business Combinations with Interested Shareholders

Our Articles of Association provide that, subject to certain exceptions, we may not engage in certain business combinations with any person that acquires beneficial ownership of 15% or more of our outstanding voting shares for a period of three years following the date on which the person became a 15% shareholder unless: (i) prior to the date on which the person becomes a 15% shareholder, a committee of our disinterested directors approved the business combination; and (ii) in certain circumstances, the business combination is authorized by a special resolution of disinterested shareholders.

Further Provisions

Certain other provisions of Irish law or our Constitution may be considered to have anti-takeover effects, including advance notice requirements for director nominations and other shareholder proposals, as well as those described under the headings "—Capital Structure - Authorized Share Capital" (regarding issuance of preferred shares), "—Pre-emption Rights, Share Warrants and Share Options," "—Disclosure of Interests in Shares," "—Appointment of Directors," and "—Removal of Directors."

Insider Dealing

Irish Takeover Rules also provide that no person, other than the bidder, who is privy to confidential price-sensitive information concerning an offer made in respect of the acquisition of a company (or a class of its securities) or a contemplated offer shall deal in relevant securities of the target during the period from the time at which such person first has reason to suppose that such an offer, or an approach with a view to such an offer being made, is contemplated to the time of (i) the announcement of such offer or approach or (ii) the termination of discussions relating to such offer, whichever is earlier.

Corporate Governance

Our Articles of Association allocate authority over the day-to-day management of the Company to the board of directors. Our board of directors may then delegate management of the Company to committees of the board or such other persons as it thinks fit. Regardless of any delegation, the board of directors will remain responsible, as a matter of Irish law, for the proper management of the affairs of our Company. The board of directors may create new committees or change the responsibilities of existing committees from time to time. Committees may meet and adjourn as they determine proper. Unless otherwise determined by the board of directors, the quorum necessary for the transaction of business at any committee meeting shall be a majority of the members of the committee.

Appointment of Directors

The Irish Companies Act provides for a minimum of two directors. Our Articles of Association provide that the number of directors will be not less than two and not more than 13. The authorized number of directors within the prescribed range will be determined solely by our board of directors and does not require approval or ratification by the shareholders in a general meeting. Our directors will be elected by way of an ordinary resolution at a general meeting save that directors in contested elections will be elected by a plurality of the votes of the shares present in person or represented by proxy at the relevant general meeting and entitled to vote on the election of directors. If the number of the directors is reduced below the fixed minimum number, the remaining director or directors may appoint an additional director or additional directors to make up such minimum or may convene a general meeting for the purpose of making such appointment. Casual vacancies may be filled by the board of directors.

Our Articles of Association provide that our board of directors is divided into three classes serving staggered three-year terms. Shareholders do not have cumulative voting rights. Accordingly, the holder of a majority of the voting rights attaching to our ordinary shares will, as a practical matter, be entitled to control the election of all directors. At each annual general meeting, directors will be elected for a full term of three years to succeed those directors of the relevant class whose terms are expiring.

Under our Articles of Association, our board of directors has the authority to appoint directors to the board either to fill a vacancy or as an additional director. A vacancy on the board of directors created by the removal of a director may be filled by an ordinary resolution of the shareholders at the meeting at which such director is removed and, in the absence of such election or appointment, the remaining directors may fill the vacancy. The board of directors may fill a vacancy by an affirmative vote of a majority of the directors constituting a quorum. If there is an insufficient number of directors to constitute a quorum, the board of directors may nonetheless act to fill such vacancies or call a general meeting of the shareholders. Under our Articles of Association, if the board of directors 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 of directors 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 the intention to move any such resolution be given by the shareholders to the company not less than 28 days before the meeting at which the director is to be removed, and the director will be entitled to be heard at such meeting. The power of removal is

without prejudice to any claim for damages for breach of contract (e.g., employment agreement) that the director may have against us in respect of his or her removal.

Director Interested Transactions

Under the Irish Companies Act and our Articles of Association, a director who has an interest in a proposal, arrangement or contract is required to declare the nature of his or her interest at the first opportunity either (i) at a meeting of the board of directors at which such proposal, arrangement or contract is first considered (provided such director knows this interest then exists, or in any other case, at the first meeting of the board of directors after learning that he or she is or has become so interested) or (ii) by providing a general notice to the directors declaring that he or she is to be regarded as interested in any proposal, arrangement or contract with a particular person, and after giving such general notice will not be required to give special notice relating to any particular transaction. Provided the interested director makes such required disclosure, he or she shall be counted in determining the presence of a quorum at a meeting regarding the relevant proposal, arrangement or contract and will be permitted to vote on such proposal, arrangement or contract.

Pursuant to our Articles of Association, it is within the directors' sole discretion to determine their compensation.

Borrowing

Pursuant to our Articles of Association, among the directors' powers are the right to borrow money and to mortgage or charge the Company's undertaking, property and uncalled capital or any part thereof and to issue debentures, debenture shares, mortgages, bonds or such other securities whether outright or as security for any debt, liability or obligation of the Company or of any third party.

Duration; Dissolution; Rights upon Liquidation

Our duration will be unlimited. We may be dissolved and wound up at any time by way of a shareholders' voluntary winding up or a creditors' winding up. In the case of a shareholders' voluntary winding-up, a special resolution of shareholders is required. We may also be dissolved by way of court order on the application of a creditor, or by the Companies Registration Office as an enforcement measure where we have failed to file certain returns. We may also be dissolved by the Irish Corporate Enforcement Authority where the affairs of the Company have been investigated by an inspector and it appears from the report or any information obtained by the Irish Corporate Enforcement Authority that we should be wound up.

The rights of the shareholders to a return of our assets on dissolution or winding up, following the settlement of all claims of creditors, are prescribed in our Articles of Association or the terms of any shares issued by the directors from time to time. The holders of preferred shares in particular may have the right to priority in a dissolution or winding up. If the Articles of Association and terms of issue of the shares of the Company contain no specific provisions in respect of a dissolution or winding up then, subject to the shareholder priorities and the rights of any creditors, the assets will be distributed to shareholders in proportion to the paid-up nominal value of the shares held. Our Articles of Association provide that our ordinary shareholders may be entitled to participate in a winding up, and the method by which the property will be divided shall be determined by the liquidator, subject to a special resolution of the shareholders, but such rights of ordinary shareholders to participate may be subject to the rights of any preferred shareholders to participate under the terms of any series or class of preferred shares.

Share Certificates

Pursuant to the Irish Companies Act, a shareholder is entitled to be issued a share certificate on request and subject to payment of a nominal fee.

Stock Exchange Listing

Our ordinary shares are listed on the Nasdaq Capital Market under the symbol "ITRM." Our ordinary shares are not listed on Euronext Dublin.

No Sinking Fund

Our shares have no sinking fund provisions.

Transfer and Registration of Shares

Our transfer agent is Computershare Trust Company, N.A. The transfer agent maintains our share register, and registration in the share register will be determinative of membership in us. A shareholder of ours who only holds shares beneficially will not be the holder of record of such shares. Instead, the depository or other nominee will be the holder of record of those shares. Accordingly, a transfer of shares from a person who holds such shares beneficially to a person who also holds such shares beneficially through a depository or other nominee will not be registered in our official share register, as the depository or other nominee will remain the record holder of any such shares.

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

Any transfer of our shares that is subject to Irish stamp duty will not be registered in the name of the buyer unless an instrument of transfer is duly stamped and provided to our transfer agent. Our Articles of Association allow us, in our absolute discretion, to create an instrument of transfer and pay (or procure the payment of) any stamp duty, which is the legal obligation of a transferee. In the event of any such payment, we are (on behalf of ourselves or our affiliates) entitled to (i) seek reimbursement from the transferee or transferor (at its discretion), (ii) set-off the amount of the stamp duty against future dividends payable to the transferee or transferor (at its discretion) and (iii) have a lien against the shares on which it has paid stamp duty. Parties to a share transfer may assume that any stamp duty arising in respect of a transaction in our shares has been paid unless one or both of such parties is otherwise notified by us.

Our Articles of Association delegate to our secretary (or such other person as may be nominated by the secretary for this purpose) the authority to execute an instrument of transfer on behalf of a transferring party.

Our Articles of Association grant our board of directors general discretion to decline to register an instrument of transfer unless the transfer is in respect of one class of shares only, the instrument of transfer is accompanied by the certificate of shares to which it relates (if any) and such other evidence as the directors may reasonably require to show the right of the transferor to make the transfer, the instrument of transfer is in favor of not more than four transferees and it is lodged at our registered office or such other place as our directors or secretary may appoint.

The directors may suspend registration of transfers from time to time, not exceeding 30 days in aggregate each year, as our board of directors may from time to time determine (except as may be required by law).

EXHIBIT 10.22

Dated December 5, 2024

ITERUM THERAPEUTICS INTERNATIONAL LIMITED

-and-

MICHAEL DUNNE

AMENDMENT TO CONTRACT FOR SERVICES

THIS AMENDMENT to a CONTRACT FOR SERVICES is made and entered into on December 5, 2024, by and between:

(1) **ITERUM THERAPEUTICS INTERNATIONAL LIMITED** whose registered office is at Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, D02 YW24, Ireland (the **Company**); and

(2) **MICHAEL DUNNE** of 30 Cromwell Place, Old Saybrook, CT, 06475 (the **Contractor**),

ereinafter referred to as **Amendment No.5**.

The Company and the Contractor are hereinafter individually referred to as a **Party** or collectively referred to as the **Parties**.

RECITALS

A.The Parties entered into a Contract for Services dated May 25, 2022, pursuant to which the Contractor agreed to provide the Services to the Company and any Associated Company upon and subject to the terms and conditions therein contained (the **Consultancy Agreement**), a copy of which is attached hereto in Schedule 1.

B.The Parties entered into an Amendment Agreement dated December 31, 2022, pursuant to which the Parties agreed to extend the Term of the Consultancy Agreement until June 30, 2023, upon and subject to the terms and conditions therein contained (**Amendment No.1**), a copy of which is attached hereto in Schedule 2.

C.The Parties entered into an Amendment Agreement dated June 15, 2023, pursuant to which the Parties agreed to extend the Term of the Consultancy Agreement until December 31, 2023, upon and subject to the terms and conditions therein contained (**Amendment No.2**), a copy of which is attached hereto in Schedule 3.

D.The Parties entered into an Amendment Agreement dated June 15, 2023, pursuant to which the Parties agreed to extend the Term of the Consultancy Agreement until June 30, 2024, upon and subject to the terms and conditions therein contained (**Amendment No.3**), a copy of which is attached hereto in Schedule 4.

E.The Parties entered into an Amendment Agreement dated August 9, 2024, pursuant to which the Parties agreed to extend the Term of the Consultancy Agreement until December 31, 2024, upon and subject to the terms and conditions therein contained (**Amendment No.4**), a copy of which is attached hereto in Schedule 5.

F.The Parties hereto wish to further amend the Consultancy Agreement as prescribed herein, effective as of December 31, 2024 (the **Amendment Effective Date**).

IT IS HEREBY AGREED as follows:

1.EXISTING TERMS, CONDITIONS AND DEFINITIONS

1.1.Unless specifically amended herein, the terms and conditions described in the Consultancy Agreement shall remain in full force and effect.

1.2.Capitalised terms (including those used in the Recitals above) shall be as defined in the Consultancy Agreement, Amendment No.1, Amendment No.2, Amendment No.3 and Amendment No.4.

2.TERM

2.1.Clause 3.1 (“Term”) of the Consultancy Agreement shall be amended to read as follows:

> “*This Agreement commenced on the Commencement Date and continues until 30 June 2025 unless earlier terminated in accordance with clause 3.2 or clause 14. The Term may be extended by mutual agreement of the parties.*”

3.AMENDMENT

3.1.All references to “Agreement”, “hereunder”, “herein”, “hereof” or similar words referring to the Consultancy Agreement, from and after the Amendment Effective Date, shall mean and refer to the Consultancy Agreement as amended by this Amendment No.5.

4.COUNTERPARTS

4.1.This Amendment No.5 may be executed in any number of counterparts, and by the Parties on separate counterparts, each of which when so executed will constitute an original but all of which together will evidence the same agreement.

IN WITNESS whereof this Amendment No.5 has been entered into on the date first herein written.

SIGNED on behalf of the Company:

/s/ Corey Fishman

…….....
Signature

Name: Corey Fishman

Title: Director

SIGNED By Contractor:

/s/ Michael Dunne

…….....
Signature

Name: Michael Dunne

SCHEDULE 1

THE CONSULTANCY AGREEMENT

Dated May 25, 2022

ITERUM THERAPEUTICS INTERNATIONAL LIMITED

-and-

MICHAEL DUNNE

CONTRACT FOR SERVICES

THIS AGREEMENT is dated May 25, 2022 and made between:

(1) **ITERUM THERAPEUTICS INTERNATIONAL LIMITED** whose registered office is at Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, DO2 YW24, Ireland (the **Company**); and

(2) **MICHAEL DUNNE** of 30 Cromwell Place, Old Saybrook, CT, 06475 (the **Contractor**)

ereinafter referred to as the **Agreement**.

RECITAL

The Contractor has agreed to provide the Services to the Company and any Associated Company upon and subject to the terms and conditions hereinafter contained.

IT IS HEREBY AGREED as follows:

5.DEFINITIONS AND INTERPRETATION

5.1.In this Agreement, unless the context otherwise requires:

Associated Company means any holding company or any subsidiary of the Company (as such terms are defined by section 7 and section 8 of the Companies Act, 2014) or any subsidiary of such holding company;

Board means the Board of Directors of Iterum Therapeutics plc;

Business of the Company means development and commercialization of therapies focused on patients with infectious diseases and other acute illnesses. Our lead product candidate, sulopenem, is in development for the treatment of patients with uncomplicated urinary tract infections (uUTI) associated primarily with resistant gram-negative bacteria;

Business Day means any day on which banks are generally open for business in Dublin;

Business Opportunities means any opportunities which the Contractor becomes aware of during the course of the Agreement which relates to the Business of the Company**;**

Capacity means as agent, contractor, director, employee, owner, partner, and shareholder or in any other capacity;

Commencement Date means May 1, 2022;

Companies mean the Company and any Associated Company or any of them;

Company Property means all documents, books, records, correspondence, papers and information (on whatever media and wherever located) relating to the Business of the Company or its customers and business contacts including any equipment, keys, hardware or software provided to the Contractor during the term of the Agreement and any data or documents (including copies) produced, maintained or stored by the Contractor for the Company on the Contractor's computer systems or other electronic equipment during the Agreement;

Confidential Information means any and all information received or obtained as a result of entering into or performing, or supplied by or on behalf of a party in the negotiations leading to, this Agreement and which relates to:-

(a) the Companies;

(b) any aspect of any Business of the Companies;

(c) the provisions of this Agreement;

(d) the negotiations relating to this Agreement; or

(e) the subject matter of this Agreement.

FDA means the United States Food and Drug Administration;

Fees mean the remuneration payable by the Company to the Contractor for the provision of the Services in accordance with clause 4 and Schedule 1;

Force Majeure means, in relation to either party, any circumstances beyond the reasonable control of that party (including, without limitation, any strike, lock-out or other form of industrial action);

Intellectual Property Rights means patents, rights to invention, copyright and related rights, trademarks, trade names and domain names, rights in get-up, rights in goodwill or to sue for passing off, unfair competition rights, rights in designs, rights in computer software, database rights, topography rights, rights in confidential information (including know-how and trade secrets) and any other intellectual property rights, in each case whether registered or unregistered and including all applications (or rights to apply) for, and renewals or extensions of, such rights and all similar or equivalent rights or forms of protection which subsist or will subsist now or in the future in any part of the world;

Inventions means any invention, idea, discovery, development, improvement or innovation made by the Contractor in connection with the provision of the Services, whether or not patentable or capable of registration, and whether or not recorded in any medium;

Month means calendar month; and

NDA means a new drug application (or any successor form or application having substantially the same effect with respect to the approval of a drug for marketing and sale);

Term shall have the meaning given to that term in clause 3, as may be extended for time to time.

Services means the Services specified in Schedule 2 to this Agreement.

Works means all records, reports, documents, papers, drawings, designs, transparencies, photos, graphics, logos, software programmes, inventions, ideas, discoveries, developments, improvements or innovations and all materials embodying them in whatever form prepared by the Contractor or Individual in connection with the provision of the Service.

5.2. The Schedules referred to in this Agreement form an integral part of this Agreement, and references to this Agreement include reference to the Schedules.

5.3. All references in this Agreement to costs, charges or expenses include any value added tax or similar tax charged or chargeable on them.

5.4. Unless the context otherwise requires, in this Agreement:

5.4.1. words denoting the singular include the plural and vice versa and words importing the masculine include the feminine;

5.4.2. references to Acts, statutory instruments and other legislation are to legislation operative in Ireland and to such legislation, modified, consolidated, amended or re-enacted (whether before or after the date of this Agreement) and any subordinate legislation made under that legislation;

5.4.3.reference to any Irish legal term, concept, legislation or regulation (including, without limitation, those for any action, remedy, method of judicial proceeding, document, statute, court official, governmental authority or agency) or any accounting term or concept, in respect of any jurisdiction other than Ireland is construed as a reference to the term or concept which most nearly corresponds to it in that jurisdiction; and

5.4.4.reference to any document includes that document as amended or supplemented whether before or after the date of this Agreement.

6.APPOINTMENT OF CONTRACTOR

6.1.The Company hereby appoints the Contractor to provide the Services to the Companies during the term of this Agreement, and the Contractor shall act in that capacity subject to the terms and conditions of this Agreement.

7.TERM

7.1.This Agreement commenced on the Commencement Date and continues until 31 December 2022 unless earlier terminated in accordance with clause 3.2 or clause 14. The Term may be extended by mutual agreement of the parties.

7.2.Subject to clause 14, either party may terminate this Agreement on not less than two months' notice in writing to the other party and the termination date shall be the expiry of the notice period.

8.FEES

8.1.The Company shall pay to the Contractor the Fees set out in Schedule 1 within 7 days of receipt of the Contractor's invoice therefor to such bank account as the Contractor may from time to time notify in writing to the Company. Invoices shall be furnished by the Contractor monthly in arrears on the last day of each month and will be payable by the Company 7 days from the date of the invoice.

9.DUTIES AND OBLIGATIONS OF CONTRACTOR

9.1.The Contractor shall provide the Services on such days as are required and agreed in writing by the Company from time to time and in consideration of the Contractor working such days will be remunerated in accordance with Clause 4.1 above.

9.2.The Contractor shall:

5.2.1. provide the Services with all due care, skill and ability and use his best endeavours to promote the interests of the Company;

5.2.2. promptly give to the Company all such information and reports as it may reasonably require in connection with matters relating to the provision of the Services or the Business of the Company

9.3.If the Contractor is unable to provide the Services due to illness or injury, the Contractor shall advise the Company of that fact as soon as reasonably practicable. For the avoidance of doubt, no fee shall be payable in accordance with clause 4 in respect of any period during which the Services are not provided.

9.4.Unless specifically authorised to do so by the Company:

9.4.1.The Contractor shall not have any authority to incur any expenditure in the name of or for the account of the Company; and

9.4.2.The Contractor shall not hold himself out as having authority to bind the Company

9.5.The Contractor undertakes to comply with all reasonable standards of safety and comply with the health and safety procedures of the Company from time to time in force at the premises where the Services are provided and report to the Company any unsafe working conditions or practices.

9.6.The Contractor undertakes during the appointment to take all reasonable steps to offer (or cause to be offered) to the Company any Business Opportunities as soon as practicable after the same shall have come to its or his knowledge and in any event before the same shall have been offered by the Contractor (or caused to be offered) to any other party.

9.7.The Contractor may use a third party to perform any administrative, clerical or secretarial functions which are reasonably incidental to the provision of the Services provided that the Company will not be liable to bear the cost of such functions.

9.8.The Contractor shall:

9.8.1.comply with all applicable laws, regulations, codes and sanctions relating to anti-bribery and anti-corruption in Ireland or in any other jurisdiction in relation to which work is undertaken;

9.8.2.comply with any Ethics and Anti-bribery and Anti-corruption Policies of the Company and any relevant industry code in force from time to time (Relevant Policies);

9.8.3.promptly report to the Company any request or demand for any undue financial or other advantage of any kind received by the Contractor in connection with the performance of this Agreement; and

9.8.4.ensure that all persons associated with the Contractor who are performing services in connection with this Agreement comply with this clause 5.8.

9.9.Breach of clause 5.8 shall be deemed a material breach of this Agreement.

9.10.The Contractor shall be responsible for all property of the Companies in his possession.

9.11.The Contractor shall obtain all necessary licences, certificates, permits, consents and authorisations from all relevant government departments, agencies or regulatory authorities to enable it to perform and carry out is obligations under or pursuant to this Agreement.

9.12.The Contractor shall comply with all relevant environmental and safety legislation and shall comply with all legal requirements from time to time in force relating to the Services.

9.13.The Contractor shall from time to time consult with representatives of the Companies for the purpose of assessing the quality of the Services and obtaining feedback.

9.14.The Contractor will provide the Company with copies of all necessary documentation, including all and any delivery dockets, route sheets, cash receipts, settlement sheets, cash summaries and other documentation required by the Company for the orderly completion of the Contractor’s duties relating to the Services provided by the Contractor under this Agreement.

10.EXPENSES

10.1.The Company shall reimburse all reasonable expenses properly and necessarily incurred by the Contractor in the course of the appointment, subject to the Contractor seeking prior consent from the Company to incur such expenditure and the production of receipts or other appropriate evidence of payment.

10.2.If the Contractor is required to travel abroad in the course of the appointment the Contractor shall be responsible for any necessary insurances, inoculations and immigration requirements. For the avoidance of doubt, the Company shall discharge the flight and accommodation costs excluding subsistence costs associated with the Contractor's requirement to travel under this agreement.

11.OTHER ACTIVITIES

11.1.Nothing in this Agreement shall prevent the Contractor from being engaged, concerned or having any financial interest in any Capacity in any other business, trade, profession or occupation during the appointment provided that:

11.1.1.such activity does not cause a breach of any of the Contractor's obligations under this Agreement; and

11.1.2.the Contractor shall not engage in any such activity if it relates to a business which is similar to or in any way competitive with the Business of the Company or Companies, without the prior written consent of the Company and the Contractor agrees to give priority to the provision of the Services to the Company over any other business activities undertaken by it during the course of the appointment.

12.CONFIDENTIAL INFORMATION & COMPANY PROPERTY

12.1.The parties agree that the terms of this Agreement are confidential to the parties and their professional advisors.

12.2.The Contractor acknowledges that prior to, and in the course of, the appointment he will have access to Confidential Information. The Contractor has therefore agreed to accept the restrictions in this clause 8 which will continue to apply after the termination or expiry of the Agreement.

12.3.The Contractor shall not (except in the proper course of his duties), between signing this Agreement and the date of its commencement, during the appointment or at any time after the termination date, use or disclose to any third party (and shall use his reasonable endeavours to prevent the publication or disclosure of) any Confidential Information. This restriction does not apply to:

12.3.1.any use or disclosure authorised by the Company or required by law; or

12.3.2.any information which is already in, or comes into, the public domain otherwise than through the unauthorised disclosure of the Contractor;

12.4.At any stage during the appointment, the Contractor will promptly on request return all and any Company Property in his possession.

13.INTELLECTUAL PROPERTY

13.1.The Contractor shall give the Company full written details of all Inventions and of all works embodying Intellectual Property Right made wholly or partially by the Contractor, or any appointed substitute (as the case may be) at any time during the course of this Agreement which relate to, or are reasonably capable of being used in the Business of the Company.

13.2.The Contractor acknowledges that all Intellectual Property Rights subsisting in any work or Invention made, originated or developed by the Contractor or any appointed substitute (as the case may be) at any time in relation to the Services shall automatically on creation, vest in and be the absolute sole and unencumbered property of the Company. To the extent that the Intellectual Property Rights do not vest automatically with the Company the Contractor holds them on trust

for the Company. The Contractor hereby agrees to execute or to procure the execution of all such documents to make such applications and give such assistance as may in the opinion of the Company be necessary to give effect to this clause.

13.3. The Contractor hereby irrevocably waives all moral rights under the Copyright and Related Rights Act 2000 to 2007 (and all similar rights in other jurisdictions) which the Contractor has or will have in any existing or future works referred to in this clause.

13.4. The Contractor irrevocably appoints the Company or its nominee to be its attorney to execute in its name and on its behalf any document or instrument for the purpose of giving the Company or its nominee the benefit of this clause. The Contractor acknowledges in favour of any third party that a certificate in writing signed by the Company that any instrument or act falls within the authority conferred by this clause shall be conclusive evidence that such is the case.

13.5. The Contractor acknowledges that no further remuneration or compensation other than that provided for in this Agreement is or may become due to the Contractor in respect of the performance of its obligations under this clause 9.

14. DATA PROTECTION

14.1. All personal information which the Company holds about the Contractor is protected by data protection laws. The Company will collect and process personal data relating to employees in accordance with the privacy notice which is attached at Schedule 3.

15. WARRANTIES AND REPRESENTATIONS

15.1. The Contractor warrants and represents that it has full capacity and authority to enter into and perform this Agreement.

15.2. The Contractor warrants and represents that the Contractor will carry out the Services in a good and workmanlike manner and:

15.2.1. that the Contractor has the necessary skill to render the Services;

15.2.2. that the Contractor will supply the Services with due skill, care and diligence;

15.2.3. that, where materials are used, they will be sound and reasonably fit for the purpose for which they are required; and

15.2.4. that, where goods are supplied under this Agreement, they will be of merchantable quality within the meaning of section 4(3) of the Sale of Goods Act 1893.

15.3. The Contractor warrants and represents that, in connection with the provision of the Services under this Agreement, it will at all times:

15.3.1. maintain all necessary licences, certificates, permits, consents and authorisations from all relevant government departments, agencies or regulatory authorities;

15.3.2. comply in all material respects with all relevant environmental and safety legislation; and

15.3.3. comply with all legal requirements from time to time in force relating to the Services and the provision of them.

15.4. The Contractor warrants and represents that it will at all times conduct its business in a manner that shall reflect favourably on the Companies, the Services and the good name and reputation of the Companies.

16.INDEMNITY

16.1.The Contractor shall indemnify and keep indemnified the Companies their respective officers, directors and employees from and against any and all loss, damage or liability (whether criminal or civil) suffered and legal fees and costs incurred, resulting from:

16.1.1. any breach of this Agreement by the Contractor, its employees or agents; and

16.1.2.any act, neglect or default of the Contractor, its employees or agents.

17.LIMITATION OF LIABILITY

17.1.Notwithstanding anything to the contrary in this Agreement, the Company will not (except in respect of death or personal injury caused by any negligent act or omission of the Company) be liable to the Contractor by reason of any representation or implied warranty, condition or other term or any duty at common law, or under the express terms of this Agreement for any consequential loss or damage (whether occasioned by the negligence of the Company, its employees or agents) or otherwise arising out of or in connection with this Agreement.

18.TERMINATION

18.1.Either party may terminate this Agreement in accordance with clause 3.

18.2.The Company will be entitled to terminate this Agreement by giving not less than 7 days' written notice to the Contractor if the Contractor at any time challenges the validity of any intellectual property rights of the Companies.

18.3.The Company will be entitled forthwith to terminate this Agreement by written notice to the Contractor if:

18.3.1.the Contractor commits any breach of any of the provisions of this Agreement and, in the case of a breach capable of remedy, fails to remedy the same within 30 days after receipt of a written notice giving full particulars of the breach and requiring it to be remedied;

18.3.2.an encumbrancer takes possession of or a receiver is appointed over any of the property or assets of the Contractor;

18.3.3.the Contractor makes any voluntary arrangement with its creditors or becomes subject to an administration order;

18.3.4.the Contractor is declared bankrupt;

18.3.5.anything analogous to any of the foregoing under the law of any jurisdiction occurs in relation to the Contractor;

18.3.6.the Contractor is incapacitated from carrying on the Service for an aggregate period of 150 days in any 52-week period;

18.3.7.the Contractor is convicted of any criminal offence (other than an offence under the road traffic legislation) in Ireland or elsewhere for which a non-custodial penalty is imposed;

18.3.8.the Contractor is, in the reasonable opinion of the Board of the Company, negligent or incompetent in the performance of the Services; or

18.3.9.the Contractor, ceases or threatens to cease, to carry on business.

18.4.For the purposes of clause 14.3.1, a breach will be considered capable of remedy if the party in

breach can comply with the provision in question in all respects other than as to the time of performance (provided that time of performance is not of the essence).

18.5.Subject as otherwise provided herein and to any rights or obligations which have accrued prior to termination, neither party will have any further obligation to the other under this Agreement.

19.CONSEQUENCES OF TERMINATION

19.1.Upon the termination or expiry of this Agreement for any reason:

19.1.1.the Contractor shall cease to provide the Services;

19.1.2.the Contractor shall immediately return to the Company all the Companies' property held by the Contractor or under his control;

19.1.3.the provisions of clauses 8, 9, 17 and this clause 15 will continue in force in accordance with their respective terms;

19.1.4.the Contractor shall cease to refer to himself as being in any way affiliated or associated with the Company;

19.1.5.the Contractor will have no claim against the Company for loss or profits, loss of goodwill or any other loss;

19.1.6.insofar as is reasonably possible the Contractor shall irretrievably delete any information relating to the Business of the Company or any Companies stored on any magnetic or optical disk or memory and all matter derived from such sources which is in his possession or under his control outside the premises of the Company. For the avoidance of doubt, the contact details of business contacts made during the appointment are regarded as Confidential Information, and as such, must be deleted from personal, social or professional networking accounts; and

19.1.7.provide a signed statement that it/he has complied fully with his obligations under this clause 15.

20.STATUS

20.1.The relationship of the Contractor to the Company will be that of independent contractor and nothing in this agreement shall render the Contractor an employee, worker, agent or partner of the Company. The Contractor shall have the right to control and determine the time, place, methods, manner and means of performing the Services. In performing the Services, the amount of time devoted by the Contractor on any given day will be entirely within the Contractor's control, and the Company will rely on the Contractor to put in the amount of time necessary to fulfill the requirements of this Agreement.

20.2.This Agreement constitutes a contract for the provision of services and is not a contract of employment and accordingly the Contractor shall be fully responsible for any income tax, PRSI and USC contributions and any other liability, deduction, contribution, assessment or claim arising from or made in connection with either the performance of the Services whether in Ireland or elsewhere. Further, the Contractor shall not be entitled to any benefits, coverages or privileges, including, without limitation, health insurance, social security, unemployment, medical or pension payments, made available to employees of the Company.

21.MISCELLANEOUS PROVISIONS

21.1.**Announcements:**

21.1.1.Subject to clause 17.1.2, neither party shall make any announcement to shareholders, employees, customers or suppliers, or to securities markets or other authorities or to the media or otherwise, regarding the subject-matter of this Agreement or any term or provision of it without the prior written approval of the other party to this Agreement.

21.1.2.Clause 17.1.1 will not apply if and to the extent that such announcement is required by any law or by:

(1)contractual arrangements in existence at the date of this Agreement; or

(2)any securities exchange, regulatory or governmental authority or Court having jurisdiction over the party making the announcement,

whether or not the requirement has the force of law provided that any such announcement may only be made after consultation with the other party to this Agreement.

21.1.3.The provisions and restrictions in this clause 17 will continue to apply after the termination or expiry of this Agreement.

21.1.4.If either party makes an announcement pursuant to this clause 17 shall provide a copy of that announcement to the other party to this Agreement before the announcement is made unless this is not reasonably practicable, in which case, a copy of the announcement shall be so provided to the other party as soon as reasonably practicable.

21.1.5.Each party shall provide all such information known to it or, which on reasonable enquiry ought to be known to it as may reasonably be required by the other party in relation to the Services for the purposes of complying with the requirements of the law or any securities exchange or regulatory or governmental authority having jurisdiction over the Company or the Contractor as the case may be.

22.Assignment:

22.1.Neither party to this Agreement may assign any of its rights under this Agreement without the prior written consent of the other party except that the Company may assign the benefit of any provision of this Agreement to any Associated Company without the consent of the Contractor and such assignee shall be entitled to enforce the same rights against the Contractor as if it were named as the Company under this Agreement.

22.2.Subject to clause 18.1, this Agreement will be binding on and ensure for the benefit of the permitted assigns and successors in title to each of the parties and references to the parties will be construed accordingly.

23.Costs and Expenses:

23.1.Each party to this Agreement shall pay its own costs of and incidental to this Agreement and its implementation.

24.Severability:

24.1.All the terms and provisions of this Agreement are distinct and severable, and if any term or provision is held or declared to be unenforceable, illegal or void in whole or in part by any court, regulatory authority or other competent authority, it will to that extent only, be deemed not to form part of this Agreement, and the enforceability, legality and validity of the remainder of this Agreement will not in any event be affected. However, if as a result of the operation of this clause the rights or obligations of a party are materially altered to the detriment of that party, that

party may terminate this Agreement within 30 days from the date of the relevant decision of the relevant court, regulatory authority or other competent authority.

25.Whole Agreement:

25.1.This Agreement (together with any documents to be executed pursuant to the terms of this Agreement) supersede all prior representations, arrangements, understandings and agreements, and sets out the entire, complete and exclusive agreement and understanding between the parties. The rights of the Company under this Agreement are independent, cumulative and without prejudice to all other rights available to it whether as a matter of common law, statute, custom or otherwise.

26.Forbearance and Waiver

26.1.No waiver by the Company in respect of any breach of this Agreement by the Contractor will operate as a waiver in respect of any subsequent breach. No failure or delay by the Company in exercising any right or remedy will operate as a waiver thereof, nor will any single or partial exercise or waiver of any right or remedy prejudice its further exercise or the exercise of any other right or remedy.

27.Force Majeure:

27.1.If either party is affected by Force Majeure it shall forthwith notify the other party of the nature and extent thereof.

27.2.Neither party shall be deemed to be in breach of this Agreement, or otherwise be liable to the other, by reason of any delay in performance, or non-performance of its obligations hereunder to the extent that such delay or non-performance is due to any Force Majeure of which it has notified the other party, and the time for performance of that obligation shall be extended accordingly.

27.3.If the Force Majeure in question prevails for a continuous period in excess of six months the parties shall enter into bona fide discussions with a view to alleviating its effects, or to agreeing upon such alternative arrangements as may be fair and reasonable.

28.Notices:

28.1.Any notice given under this agreement shall be in writing and signed by or on behalf of the party giving it and shall be served by delivering it personally, or sending it registered post to the Company's registered office for the time being and / or address given in this agreement in the case of the Contractor or by sending it by fax to the fax number notified by the relevant party to the other party. Any such notice shall be deemed to have been received:

28.1.1.if delivered personally, at the time of delivery;

28.1.2.in the case of registered post, 48 hours from the date of posting; and

28.1.3.in the case of fax, at the time of transmission.

28.2.In proving such service it shall be sufficient to prove that the envelope containing the notice was addressed to the address of the relevant party and delivered either to that address or into the custody of the postal authorities as registered post or that the notice was transmitted by fax to the fax number of the relevant party.

29.Variation:

29.1.No variation of this agreement or of any document referred to in it shall be valid unless it is in writing and signed by or on behalf the parties.

30.Third Party Rights:

30.1.A person/entity who is not a party to this agreement shall not have any rights under or in connection with it.

31.Counterparts:

31.1.This Agreement may be executed in any number of counterparts, and by the several parties to it on separate counterparts, each of which when so executed will constitute an original but all of which together will evidence the same agreement.

32.Governing Law:

32.1.This Agreement and all relationships created by it will in all respects be governed by and construed in accordance with Irish law.

33.Jurisdiction:

33.1.1.The Irish courts will have exclusive jurisdiction to settle any dispute (**Dispute**) which may arise out of or in connection with this Agreement or its performance.

33.1.2.The parties agree that the Irish courts are the most appropriate and convenient courts to settle any Dispute and therefore that they will not argue to the contrary.

33.1.3.This clause is for the exclusive benefit of the Company and it will not prevent the Company from initiating proceedings in relation to a Dispute (**Proceedings**) in any other court of competent jurisdiction. To the extent permitted by law, the Company may take concurrent Proceedings in any number of jurisdictions.

IN WITNESS whereof this Agreement has been entered into on the date first herein written.

SIGNED on behalf of the Company

in the presence of: Kevin Dalton

/s/ Corey Fishman

….....

Signature

Director

….....

Title

SIGNED By Contractor

in the presence of: William Dunne

/s/ Michael Dunne

….....

Signature

SCHEDULE 1

FEES

A monthly fee of $5,000 will be payable to the Contractor effective from the first full month following the Commencement Date

SCHEDULE 2

SERVICES

To provide general support and strategic advice to the Company in connection with the potential resubmission of the NDA for oral sulopenem including in connection with the design and conduct of a Phase III clinical trial to support such potential resubmission.

SCHEDULE 3

DATA PRIVACY NOTICE

Workplace Privacy Notice

1What is the purpose of this document?

This Privacy Notice describes how we collect and use personal data about you during and after your working relationship with us, in accordance with data protection law. This Privacy Notice applies to all employees, former employees, interns, agency workers and contractors.

Iterum Therapeutics International Limited, with company number 564304 and registered office at Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, Ireland ("Iterum"; "we", "us" and "our") is a **"controller"** of your employment related personal data. This means that we are responsible for deciding how we hold and use your personal data.

We use personal data that we receive as part of the recruitment and on-boarding processes, together with additional personal data we receive throughout the course of our working relationship with you (e.g. so we can pay salaries, participation in benefit schemes, performance reviews, disciplinary processes etc.). The personal data we receive is mostly processed for managing our workforce, performance of employment contracts and to comply with our legal obligations as an employer.

This Privacy Notice sets out the information that we must provide to you in accordance with Irish data protection laws, including the General Data Protection Regulation (EU) 2016/679 ("GDPR") and the Data Protection Acts 1988 to 2018, as these laws may be amended and supplemented from time to time ("data protection law"). You have certain rights in respect of your personal data, which are described in this Privacy Notice.

This Privacy Notice does not form part of any contract of employment or other contract to provide services.

It is important that you read and retain this Privacy Notice, together with any other privacy notice we may provide on specific occasions when we are collecting or processing personal data about you, so that you are aware of how and why we are using that information and what your rights are under data protection law.

2Who does this Privacy Notice apply to?

This Privacy Notice applies to individuals who work for us, whether they are employees, interns, contractors and/or agency workers. It covers personal data of former employees, and also third parties whose information you provide to us in connection with the employment relationship (e.g. your emergency contacts' and beneficiaries' personal data).

3The types of personal data we receive about you

"**Personal data**" means any information about an individual from which that person can be identified. It does not include data where the identity has been removed (anonymous data).

There are certain types of personal data which require a higher level of protection under data protection law, such as information about a person's health, ethnicity, religious beliefs, and trade union membership.

Throughout this Privacy Notice we use the term "processing" to refer to all activities involving your personal data, including collecting, handling, storing, sharing, accessing, using, transferring, erasing and disposing of it.

We will receive and process the following categories of personal data about you:

•**Recruitment / Selection Data** personal data contained in your job application; CV; record of interview; verification documentation; copies of right to work documentation; copy passport or other identification, work history, references and other personal data included in a cover letter, communications or as part of the application and selection process.

•**Professional Qualifications** such as colleges attended, professional qualifications and memberships, professional and/or academic transcripts.

•**Identity and Contact Data** such as your name, title, date of birth, addresses, telephone numbers, personal email addresses, and national identification number.

•**Your Personal Image** by way of photographs taken at business social events you attend; photographs included on our intranet, email and website; and photographs for marketing materials/communications.

•**Emergency Contact Data** such as the name and telephone number of your next of kin or the emergency contact(s) you nominate.

•**Dependent Data** such as civil/marital status, marriage certificate and dependants.

•**Work Details** such as work contact details; location of employment or workplace; employee number; job title; job description; reporting lines; working hours; your terms and conditions of employment; notification of relationship with a colleague and other personal data held for other legitimate purposes consequent to your employment/engagement with us.

•**Employment Records** such as start date and, if different, the date of your continuous employment; leaving date and your reason for leaving; holidays taken; training records; compensation history; termination arrangements (e.g. exit interview).

•**Remuneration and Benefits Data** such as salary, annual leave, pension and benefits information, participation in share or other work schemes; PPS number, PRSI number, VAT number (for certain contractors), bank account details, payroll records, time keeping records, tax status information and third party benefit recipient information.

•**Performance Management Data** such as performance assessments (including probationary assessments), feedback, appraisals, outputs from talent programs and performance management processes, and, where relevant, executive objective forms.

•**ICT Data** such as personal data related to your use of our information and communications systems including email and internet; your use of timekeeping systems and other information obtained through electronic means such as system login and access records; download and print records.

•**CCTV Data** namely your image and time of recording as captured by CCTV operated by the landlord of our business premises in and outside our business premises.

•**Access Control Data** namely access and security logs when you use any access control cards/fobs to gain entry to our offices.

•**Workplace Health and Safety Data** such as personal data obtained pursuant to safety audits, risk assessments and incident reports.

•**Disciplinary and Grievance Data** such as personal data contained in records (including correspondence, minutes of meetings, and reports) of allegations, investigations and proceedings, and their outcomes.

We may also receive and process **special categories of personal data** about you:

Special categories of personal data is personal data that reveals racial or ethnic origin, political opinions, religious or philosophical beliefs or trade union membership; genetic data; biometric data for the purpose of uniquely identifying a natural person; or data concerning health or a natural person's sex life or sexual orientation.

We limit the collection of this kind of personal data from you. Typically, we will only receive the following types:

•**Incapacity Data** such as personal data contained in your absence records, medical forms or certificates and records relating to any medical treatment, disability and workplace adjustments or accommodations.

•**Pre-employment Screening Data** namely the results of any mandatory pre- employment drug testing following a formal job offer but prior to commencing employment.

•**Intoxicant Data** namely the results of any mandatory intoxicant and/or drugs testing conducted during your employment/engagement with us.

In some cases, providing your personal data is necessary to enter into your employment contract with us, or to comply with applicable law. If you do not provide us with this personal data, we may not be able to perform our contract with you.

You may sometimes provide us with personal data relating to third parties, such as your spouse, partner, dependents and other family members, for purposes of Human Resources administration and management, including the administration of benefits and to contact your next-of-kin in case of an emergency. Before giving us this information please inform those third parties that you intend to disclose their personal data to us, the purposes for this disclosure, and that their personal data will be used by us in accordance with this Privacy Notice.

4How we collect your personal data

We receive your personal data as part of the recruitment and on-boarding process. Typically, we receive your personal data from the following sources:

•The landlord of our business premises, if you visit our business premises and if we request from our landlord a copy of any security recordings containing CCTV Data for the purposes described in paragraphs 5 and 6 below

•Third parties who conduct pre-employment drug tests on our behalf
Your named referees

Persons who recommend you for employment
Recruitment agencies
🕐

🕐

🕐
•You, as a job candidate (e.g. through employment related web forms and other direct communications with you)

Once you are working with us, we receive personal data from the following sources:

- You, the employee, intern, contractor or agency worker, in the course of job-related activities throughout the period of you working with us. For example, you will typically provide your personal data directly to your manager(s) or Human Resources contact, or through any Human Resources systems we operate, your participation in Human Resource processes, emails you send, and through written attendances from meetings you attend;

- From your colleagues and other personnel in the course of job-related activities and processes throughout the period of you working with us;

- From external third parties such as clients, business partners or regulatory bodies; medical reports and intoxicant and/or drugs tests reports from external professionals; tax authorities, insurance or benefit providers;

- Through access system and security logs when you use any of our information and communications systems, access control cards/fobs; time and attendance recording systems we operate; and

- The landlord of our business premises, if we request from our landlord a copy of any security recordings containing CCTV Data for the purposes described in paragraphs 5 and 6 below.

5Purposes for using your personal data

We will only use your personal data when the law allows or requires us to. In the majority of cases, the processing of your personal data will be justified for the legal grounds set out further below. In any event, to process your personal data, we will be relying on at least one of the following legal bases:

- processing is necessary to give effect to your **contract of employment** (for example, collecting bank account details to pay your salary, creating your information and communications systems access rights so you can carry out your duties, responding to grievances, managing beneficiary details, administering termination of employment and exit interviews);

- processing is necessary for us to comply with a **legal obligation** (e.g. administering mandatory benefits, reviewing eligibility for work, creating an employee record (including absences), addressing occupational health issues, managing professional qualifications, managing information and communications systems' security, disclosing tax data to government authorities or salary information to a national insurance scheme);

- processing is in our **legitimate interests** as a business and as your employer/contracting customer and our interests are not overridden by your interests, fundamental rights or freedoms (e.g. assessing new job opportunities, managing and securing information and communications systems' security; reviewing your performance at work, managing litigation or other legal requests).

The processing of **special categories of personal data** may be necessary in certain limited circumstances. To process a special category of personal data concerning you, we will rely on one of the following legal bases:

- In limited circumstances, your explicit consent;
- Where the processing is necessary for the purposes of exercising or performing any right or obligation which is given or imposed by law on an employer or the worker in connection with employment law or social welfare law;

•In respect of health related personal data only, the processing is necessary and proportionate for an occupational pension, retirement annuity contracts or any other pension arrangement;

•Where the processing is necessary for the purposes of preventive or occupational medicine and/or the assessment of your working capacity;

•Less commonly, we may process special categories of personal data where it is needed in relation to legal claims or where it is needed to protect your interests (or someone else's interests) and you are unable to give your consent, or where you have already made the information public.

6Legal bases for using your personal data

We have set out below a description of the ways we use your personal data, and which of the legal bases we rely on to do so. We have also identified what our legitimate interests are, where applicable. We may process your personal data for more than one lawful ground depending on the specific purpose for which it is necessary to use your personal data.

Purpose/activity	Type of personal data	Lawful basis for processing your personal data
To respond to your job application and to manage the recruitment process (e.g. assess your skills, qualifications and suitability for the role; checking you are legally entitled to work in Ireland; communicate with you about the recruitment process; communicate with your referees; keep records related to our hiring processes; comply with legal or regulatory requirements; to provide appropriate facilities and adjustments for your attendance at any interview; to obtain pre-employment drug test reports).	•Recruitment/ Selection Data •Professional Qualifications •Identity and Contact Data •Incapacity Data •Pre- employment Screening Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary for our legitimate interests (for running our business and to assess suitability of candidates). (c)Necessary to comply with a legal obligation. (d)Necessary for performance of an obligation which is imposed by law on an employer in connection with employment law. (e)Necessary for the assessment of working capacity.
Human resource management and management of our relationship with you (e.g. on-boarding staff; administering the contract we have entered into with you; recording notifications of relationship with a colleague; managing professional certifications / licenses and liaising with regulatory bodies on your behalf; education, training	•Recruitment/ Selection Data •Professional Qualifications •Identity and Contact Data •Emergency Contact Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary for our legitimate interests (for running our business and to ensure a positive, enjoyable and effective working environment for staff). (c)Necessary to comply with a legal obligation. (d)Necessary for performance of an obligation which is imposed by law on an employer in connection with employment law.

and development requirements; business reorganisations and corporate transactions; organising and running staff social events).	•Dependent Data •Your Personal Image •Work Details •Employment Records •Remuneration and Benefits Data •Performance Management Data •ICT Data •Access Control Data •Incapacity Data •Workplace Health and Safety Data •Disciplinary and Grievance Data •Intoxicant Data	(e)Necessary for the assessment of working capacity. (f)Necessary to protect the vital interests of a data subject or of another natural person where the data subject is physically or legally incapable of giving consent.
Administering payroll; paying your salary, and reimbursable expenses and bonuses; if you are an employee or deemed employee for tax purposes, deducting tax and other contributions; to administer benefits including statutory maternity pay, statutory sick pay, pensions and related family/dependant benefits, and permanent health insurance	•Identity and Contact Data •Work Details •Remuneration and Benefits Data •Incapacity Data •Disciplinary and Grievance Data •Dependent Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary to comply with a legal obligation. (c)Necessary for performance of an obligation which is imposed by law on an employer in connection with employment law. (d)Necessary for the assessment of working capacity.

Providing and administering pension, insurance, share plans and other benefits to you; enrolling you in pensions and other benefits; liaising with the trustees or managers of a pension arrangement, your pension provider and any other provider of staff benefits	•Identity and Contact Data •Work Details •Remuneration and Benefits Data •Dependent Data •Incapacity Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary to comply with a legal obligation. (c)Necessary and proportionate for an occupational pension, retirement annuity contract or any other pension arrangement.
Business management and planning, including accounting and auditing; conducting performance reviews; managing performance and determining performance requirements; making decisions about salary reviews and compensation; assessing qualifications for a particular job or task, including decisions about promotions; and managing headcount	•Identity and Contact Data •Work Details •Employment Records •Remuneration and Benefits Data •Performance Management Data •Workplace Health and Safety Data •Disciplinary and Grievance Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary for our legitimate interests (for running our business and strategic planning). (c)Necessary to comply with a legal obligation.
Securing our information and communication systems and networks; securing our business premises and the persons and property inside our business premises and/or on surrounding areas; creating employee records on our Human Resources IT systems; creating IT and building access rights; monitoring use of our information and communication systems to ensure compliance with our IT and other policies (including those specified in	•Identity and Contact Data •ICT Data •CCTV Data •Access Control Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary for our legitimate interests (for running our business and to protect our property, assets, staff and others; and ensuring compliance with our employment handbook, IT and other policies). (c)Necessary to comply with a legal obligation.

our employee handbook); ensuring network and information security, including preventing unauthorised access to our computer and electronic communications systems and preventing malicious software distribution and cyber attacks		
Marketing and business development including inclusion of your photograph in social media postings, publications and corporate websites	•Your Personal Image •Work Details	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary for our legitimate interests (for running our business and developing new business).
Creating and maintaining records relating to your absence from work (including for sickness, parental leave, discretionary leave, sabbaticals etc.)	•Identity and Contact Data •Work Details •Incapacity Data •Emergency Contact Data •Dependent Data •Workplace Health and Safety Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary to comply with a legal obligation. (c)Necessary for performance of an obligation which is imposed by law on an employer in connection with employment law. (d)Necessary for the assessment of working capacity.
Ensure your health and safety in the workplace and to assess your fitness to work, to provide appropriate workplace adjustments; ascertaining your fitness to work; complying with health and safety obligations; manage health and safety at work and report on incidents	•Identity and Contact Data •Work Details •Incapacity Data •Intoxicant Data •Workplace Health and Safety Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary to comply with a legal obligation. (c)Necessary for performance of an obligation which is imposed by law on an employer in connection with employment law. (d)Necessary for the assessment of working capacity.
Contacting family/next of kin in case of emergency	•Identity and Contact Data •Emergency Contact Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary for our legitimate interests (for running our business and protecting the interests and safety of staff).

	•Incapacity Data •Dependent Data	(c)Necessary to comply with a legal obligation. (d)Necessary to protect the vital interests of a data subject or of another natural person where the data subject is physically or legally incapable of giving consent.
Responding to and resolving grievances; investigate and respond to complaints from clients/customers/partners; conducting disciplinary and grievance processes; gathering evidence for possible grievance or disciplinary hearings; making decisions about your continued employment or engagement; making arrangements for the termination of working relationships	•Identity and Contact Data •Work Details •Employment Records •ICT Data •CCTV Data •Access Control Data •Workplace Health and Safety Data •Incapacity Data •Intoxicant Data •Disciplinary and Grievance Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary for our legitimate interests (for running our business and dealing effectively with grievances and disciplinary matters). (c)Necessary to comply with a legal obligation. (d)Necessary for performance of an obligation which is imposed by law on an employer in connection with employment law. (e)Necessary for the assessment of working capacity.
Dealing with legal disputes involving you, or other employees, workers and contractors, including accidents at work; to prevent fraud; conduct or assist with internal, government, law enforcement and other investigations	•Recruitment/ Selection Data •Professional Qualifications •Identity and Contact Data •Work Details •Employment Records •Remuneration and Benefits Data •Performance Management Data	(a)Performance of a contract with you, or in order to take steps at your request prior to entering into a contract. (b)Necessary for our legitimate interests (for running our business and to protect our property, assets, workforce and others). (c)Necessary to comply with a legal obligation. (d)Necessary for the establishment, exercise or defence of legal claims.

	•Workplace Health and Safety Data •Disciplinary and Grievance Data •ICT Data •Dependent Data •CCTV Data •Access Control Data •Intoxicant Data

We may operate projects or arrangements in respect of which our workforce may be invited to participate. In exceptional circumstances, depending on the nature of the project or arrangement, it may be necessary to process your personal data in respect of which we need your consent. If your consent is needed, we will ask you for this separately to ensure that your consent is freely given, informed and explicit. Information regarding processing based on your consent will be provided to you at the time that consent is requested, along with details of any consequences of not providing consent.

We will only use your personal data for the purposes for which we collected it, unless we reasonably consider that we need to use it for another reason and that reason is compatible with the original purpose. If we need to use your personal data for an unrelated purpose, we will notify you and we will explain the legal basis which allows us to do so. Please note that we may process your personal data without your knowledge or consent, in compliance with the above rules, where this is required or permitted by law.

7Disclosures of your personal data

We may have to share your personal data with third parties, including third-party service providers and with other companies that are in the same corporate group as us (e.g. our holding company and our subsidiaries, and subsidiaries of our holding company). We require third parties to respect the security of your personal data and to treat it in accordance with applicable data protection law.

Except as set out in this Privacy Notice, we do not disclose to any third party personal data that we collect or you provide to us. We will share your personal data with third parties where required by law, where it is necessary to administer the working relationship with you or where we have a legitimate interest or other lawful reason for doing so.

We may have to share your personal data with the parties set out below for the purposes set out in the table in paragraphs 5 and 6 above.

•**Internal third parties:** We will share your personal data with other companies that are in the same corporate group as us:

(i)for global Human Resources planning and decision making, we will share some of your personal data with Iterum Therapeutics US Limited in the United States, which will be a joint controller of your personal data;

(ii)for the purposes of administering the Iterum employee share option plan, we will share some of your personal data with our parent company, Iterum Therapeutics plc;

(iii)for the provision of senior executive and management services, we will share your personal data with Iterum Therapeutics US Limited in the United States who provides us with the following senior executive and management services: Human Resources management;

(iv)for the provision of information and communications systems, maintenance and support and hosting of data, for example we will share your personal data with Iterum Therapeutics US Limited who provide us with the following services: IT services; hosting, access management, security and support of desktop applications, email services and other information and communication systems we make available to you;

(v)for certain Human Resources, payroll, benefits and administrative purposes. For example, we will share your personal data with Iterum Therapeutics US Limited who provides us with the following services in respect of our workforce's personal data: payroll and financial administration services; staff training; administration of staff pensions and benefits; Human Resource support; and

(vi)in the context of a business reorganisation or a restructuring exercise.

•**External third parties:** We may share some of your personal data with professional advisors and companies that provide products and services to us. For example, the following activities are carried out by professional advisors and third-party service providers, which may involve their processing of your personal data in respect of the service they provide: pension administration and consultancy; benefits provision and administration; health insurance; IT services; cloud hosting services; employee share option plan administration; transfer agency services; payroll services; and legal and accounting services. Further, if you undergo a mandatory intoxicant and/or drugs test during your employment/engagement with us we will share your personal data with third parties who conduct these tests on our behalf.

•**Public and Government Authorities**: We may need to share your personal data with a regulator or to otherwise comply with the law. This may include making returns to Revenue.

•**Corporate activity:** We may share your personal data with other third parties in the context of the possible sale or restructuring of the business. In this circumstance we will, so far as possible, share anonymised data with the other parties before the transaction completes. Once the transaction is completed, we will share your personal data with the other parties if and to the extent required under the terms of the transaction.

We require all third parties to whom we disclose personal data to respect the security of personal data and to treat it in accordance with the law. We do not allow our service providers to use your personal data for their own purposes and only permit them to process your personal data for specified purposes and in accordance with our instructions. Unless prevented by applicable law, we will notify you when your personal data may be provided to third parties in ways other than explained above, and you may have the option to prevent this sharing at the time that we notify you.

8 International transfers

As a multinational organisation there are times we will transfer your personal data outside the European Economic Area. If we do, you can expect a similar degree of protection in respect of your personal data.

We will transfer the personal data we collect about you to the United States, which is outside of the European Economic Area, for the purposes described in paragraphs 5 and 6 and to the recipients described in paragraph 7. There is not an adequacy decision by the European Commission in respect of the United States. This means that the United States is not deemed to provide an adequate level of protection for your personal data. However, to ensure that your personal data does receive an adequate level of protection we have put in place appropriate measures, namely the European Commission approved model contractual clauses, to ensure that your personal data is treated by those third parties in a way that is consistent with and which respects data protection law. If you require further information about this protective measure you can request it from Privacy@iterumtx.com.

9 Data security

We have put in place measures to protect the security of your personal data. Details of these measures are available upon request. Third party service providers will only process your personal data on our instructions and where they have agreed to treat the information confidentially and to keep it secure.

We have put in place appropriate security measures to prevent your personal data from being accidentally lost, used or accessed in an unauthorised way, altered or disclosed. In addition, we limit access to your personal data to those employees, agents, contractors and other third parties who have a business need to know. Whilst we take appropriate security measures to protect all personal data, no data transmission or security system can be guaranteed to be 100% secure. Service providers will only process your personal data on our instructions and they are subject to obligations of confidentiality. All our third-party service providers are required to take appropriate security measures to protect personal data.

We have put in place procedures to deal with any suspected personal data breach and will notify you and the Data Protection Commission of a suspected breach where we are legally required to do so. If you have reason to believe that any of your personal data is no longer secure, please notify Privacy@iterumtx.com immediately.

You also have an important role to play in protecting the security of your personal data, and you should take care about disclosing personal data, and how you protect your communications and devices. Please refer to the employee handbook and all data protection and security policies notified to you from time to time for more information about your responsibilities and ensure you attend all mandatory data protection and data security training sessions allocated to you.

10 How long we keep your personal data

We will only retain your personal data for as long as necessary to fulfil the purposes we collected it for, including for the purposes of satisfying any legal, accounting, or reporting requirements.

To determine the appropriate retention period for personal data, we consider the amount, nature, and sensitivity of the personal data, the potential risk of harm from unauthorised use or disclosure of your personal data, the purposes for which we process your personal data and whether we can achieve those purposes through other means, and the applicable legal requirements.

In some circumstances we may anonymise your personal data so that it can no longer be associated with you, in which case we may use such information without further notice to you.

Once you are no longer an employee, worker or contractor of the company we will retain and securely destroy your personal data in accordance with applicable laws and regulations.

11Automated decision-making

Automated decision-making takes place when an electronic system uses personal data to make a decision without human intervention.

You will not be subject to decisions that will have a significant impact on you based solely on automated decision-making, unless we have a lawful basis for doing so and we have notified you. We do not envisage that any decisions will be taken about you using automated means, however we will notify you if this position changes.

12Your legal rights

Under certain circumstances, by law you have the right to:

Request access to your personal data (commonly known as a "data subject access request"). This enables you to request a copy of the personal data we hold about you and to check that we are lawfully processing it.

Request correction of the personal data that we hold about you. This enables you to have any incomplete or inaccurate personal data we hold about you corrected.

Request erasure of your personal data. This enables you to ask us to delete or remove personal data where there is no good reason for us continuing to process it. You also have the right to ask us to delete or remove your personal data where you have exercised your right to object to processing (see below).

Object to processing of your personal data where we are relying on a legitimate interest (or those of a third party) to process your personal data and there is something about your particular situation which makes you want to object to us processing your personal data on this legal ground.

Request restriction of processing of your personal data. This enables you to ask us to suspend the processing of your personal data in the following scenarios: (a) if you want us to establish the data's accuracy; (b) where our use of the personal data is unlawful but you do not want us to erase it; (c) where you need us to hold the personal data even if we no longer require it as you need it to establish, exercise or defend a legal claim; or (d) you have objected to our use of your personal data but we need to verify whether we have overriding legitimate grounds to use it.

Request the transfer of your personal data to you or to a third party. We will provide to you, or a third party you have chosen, your personal data in a structured, commonly used, machine-readable format. Note that this right only applies to automated information which you initially provided consent for us to use or where we processed the personal data to perform a contract with you.

Right to withdraw consent: In the limited circumstances where you may have provided your consent to the collection and processing of your personal data for a specific purpose, you have the right to withdraw your consent for that specific processing at any time. To withdraw your consent, please contact Privacy@iterumtx.com. Once we have received notification that you have withdrawn your consent, we will no longer process your personal data for the purpose or purposes you originally agreed to, unless we have another legitimate basis for doing so in law.

13Exercising your rights

To exercise one or more of your rights in respect of your personal data, please contact Privacy@iterumtx.com. You will not have to pay a fee to access your personal data (or to exercise any of the other personal data legal rights). However, we may charge a reasonable fee if your request for access is clearly unfounded or excessive. Alternatively, we may refuse to comply with the request in such circumstances.

14Contacting the data protection supervisory authority

You have the right to make a complaint at any time to the Data Protection Commission, the Irish supervisory authority for data protection issues (www.dataprotection.ie). We would, however, appreciate the chance to deal with your concerns before you approach the Data Protection Commission so please contact Privacy@iterumtx.com or a member of the Legal Team in the first instance.

15Updating your personal data

It is important that the personal data we hold about you is accurate and current. Please keep us informed if your personal data changes during your working relationship with us.

16Changes to this Privacy Notice

We reserve the right to update this Privacy Notice at any time. We will notify current employees in advance about any changes to this Privacy Notice that are material or may impact you.

17Who to contact?

If you have any questions about this Privacy Notice, including any requests to exercise your legal rights, please contact a member of our Privacy Team at Privacy@iterumtx.com.

I,_(employee / worker / contractor name), acknowledge that on__(date), I received a copy of this Privacy Notice for employees, workers and contractors and that I have read and understood it.

Signature

……

Name

……

SCHEDULE 2

AMENDMENT NO.1

Dated December 31, 2022

ITERUM THERAPEUTICS INTERNATIONAL LIMITED

-and-

MICHAEL DUNNE

AMENDMENT TO CONTRACT FOR SERVICES

THIS AMENDMENT to a CONTRACT FOR SERVICES is made and entered into on December 31, 2022 by and between:

(1) **ITERUM THERAPEUTICS INTERNATIONAL LIMITED** whose registered office is at Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, D02 YW24, Ireland (the **Company**); and

(2) **MICHAEL DUNNE** of 30 Cromwell Place, Old Saybrook, CT, 06475 (the **Contractor**),

ereinafter referred to as **Amendment No.1**.

The Company and the Contractor are hereinafter individually referred to as a **Party** or collectively referred to as the **Parties**.

RECITALS

A.The Parties entered into a Contract for Services dated May 25, 2022, pursuant to which the Contractor agreed to provide the Services to the Company and any Associated Company upon and subject to the terms and conditions therein contained (the **Consultancy Agreement**), a copy of which is attached hereto in Schedule 1.

B.The Parties hereto wish to amend the Consultancy Agreement as prescribed herein, effective as of December 31, 2022 (the **Amendment Effective Date**).

IT IS HEREBY AGREED as follows:

34.EXISTING TERMS, CONDITIONS AND DEFINITIONS

34.1.Unless specifically amended herein, the terms and conditions described in the Consultancy Agreement shall remain in full force and effect.

34.2.Capitalised terms (including those used in the Recitals above) shall be as defined in the Consultancy Agreement.

35.TERM

35.1.Clause 3.1 ("Term") of the Consultancy Agreement shall be amended to read as follows:

> "*This Agreement commenced on the Commencement Date and continues until 30 June 2023 unless earlier terminated in accordance with clause 3.2 or clause 14. The Term may be extended by mutual agreement of the parties.*"

36.AMENDMENT

36.1.All references to "Agreement", "hereunder", "herein", "hereof" or similar words referring to the Consultancy Agreement, from and after the Amendment Effective Date, shall mean and refer to the Consultancy Agreement as amended by this Amendment No.1.

37.COUNTERPARTS

37.1.This Amendment No.1 may be executed in any number of counterparts, and by the Parties on separate counterparts, each of which when so executed will constitute an original but all of which together will evidence the same agreement.

IN WITNESS whereof this Amendment No.1 has been entered into on the date first herein written.

SIGNED on behalf of the Company:

/s/ Corey Fishman

…..
Signature

Name: Corey Fishman

Title: Director and CEO

SIGNED By Contractor:

/s/ Michael Dunne

…..
Signature

Name: Michael Dunne

SCHEDULE 3

AMENDMENT NO.2

Dated June 15, 2023

ITERUM THERAPEUTICS INTERNATIONAL LIMITED

-and-

MICHAEL DUNNE

AMENDMENT TO CONTRACT FOR SERVICES

THIS AMENDMENT to a CONTRACT FOR SERVICES is made and entered into on June 15, 2023, by and between:

(1) **ITERUM THERAPEUTICS INTERNATIONAL LIMITED** whose registered office is at Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, D02 YW24, Ireland (the **Company**); and

(2) **MICHAEL DUNNE** of 30 Cromwell Place, Old Saybrook, CT, 06475 (the **Contractor**),

ereinafter referred to as **Amendment No.2**.

The Company and the Contractor are hereinafter individually referred to as a **Party** or collectively referred to as the **Parties**.

RECITALS

C.The Parties entered into a Contract for Services dated May 25, 2022, pursuant to which the Contractor agreed to provide the Services to the Company and any Associated Company upon and subject to the terms and conditions therein contained (the **Consultancy Agreement**), a copy of which is attached hereto in Schedule 1.

D.The Parties entered into an Amendment Agreement dated December 31, 2022, pursuant to which the Parties agreed to extend the Term of the Consultancy Agreement until June 30, 2023, upon and subject to the terms and conditions therein contained (**Amendment No.1**), a copy of which is attached hereto in Schedule 2.

E.The Parties hereto wish to further amend the Consultancy Agreement as prescribed herein, effective as of June 30, 2022 (the **Amendment Effective Date**).

IT IS HEREBY AGREED as follows:

38.EXISTING TERMS, CONDITIONS AND DEFINITIONS

38.1.Unless specifically amended herein, the terms and conditions described in the Consultancy Agreement shall remain in full force and effect.

38.2.Capitalised terms (including those used in the Recitals above) shall be as defined in the Consultancy Agreement and Amendment No.1.

39.TERM

39.1.Clause 3.1 (“Term”) of the Consultancy Agreement shall be amended to read as follows:

> “*This Agreement commenced on the Commencement Date and continues until 31 December 2023 unless earlier terminated in accordance with clause 3.2 or clause 14. The Term may be extended by mutual agreement of the parties.*”

40.AMENDMENT

40.1.All references to “Agreement”, “hereunder”, “herein”, “hereof” or similar words referring to the Consultancy Agreement, from and after the Amendment Effective Date, shall mean and refer to the Consultancy Agreement as amended by this Amendment No.2.

41.COUNTERPARTS

41.1.This Amendment No.2 may be executed in any number of counterparts, and by the Parties on separate

counterparts, each of which when so executed will constitute an original but all of which together will evidence the same agreement.
43

IN WITNESS whereof this Amendment No.2 has been entered into on the date first herein written.

SIGNED on behalf of the Company:

/s/ Corey Fishman

…..
Signature

Name: Corey Fishman

Title: Director and CEO

SIGNED By Contractor:

/s/ Michael Dunne

…..
Signature

Name: Michael Dunne

SCHEDULE 4

AMENDMENT NO.3

Dated December 27, 2023

ITERUM THERAPEUTICS INTERNATIONAL LIMITED

-and-

MICHAEL DUNNE

AMENDMENT TO CONTRACT FOR SERVICES

THIS AMENDMENT to a CONTRACT FOR SERVICES is made and entered into on December 27, 2023, by and between:

(1) **ITERUM THERAPEUTICS INTERNATIONAL LIMITED** whose registered office is at Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, D02 YW24, Ireland (the **Company**); and

(2) **MICHAEL DUNNE** of 30 Cromwell Place, Old Saybrook, CT, 06475 (the **Contractor**),

ereinafter referred to as **Amendment No.3**.

The Company and the Contractor are hereinafter individually referred to as a **Party** or collectively referred to as the **Parties**.

RECITALS

G.The Parties entered into a Contract for Services dated May 25, 2022, pursuant to which the Contractor agreed to provide the Services to the Company and any Associated Company upon and subject to the terms and conditions therein contained (the **Consultancy Agreement**), a copy of which is attached hereto in Schedule 1.

H.The Parties entered into an Amendment Agreement dated December 31, 2022, pursuant to which the Parties agreed to extend the Term of the Consultancy Agreement until June 30, 2023, upon and subject to the terms and conditions therein contained (**Amendment No.1**), a copy of which is attached hereto in Schedule 2.

I.The Parties entered into an Amendment Agreement dated June 15, 2023, pursuant to which the Parties agreed to extend the Term of the Consultancy Agreement until December 31, 2023, upon and subject to the terms and conditions therein contained (**Amendment No.2**), a copy of which is attached hereto in Schedule 3.

J.The Parties hereto wish to further amend the Consultancy Agreement as prescribed herein, effective as of December 31, 2023 (the **Amendment Effective Date**).

IT IS HEREBY AGREED as follows:

42.EXISTING TERMS, CONDITIONS AND DEFINITIONS

42.1.Unless specifically amended herein, the terms and conditions described in the Consultancy Agreement shall remain in full force and effect.

42.2.Capitalised terms (including those used in the Recitals above) shall be as defined in the Consultancy Agreement and Amendment No.1.

43.TERM

43.1.Clause 3.1 (“Term”) of the Consultancy Agreement shall be amended to read as follows:

> “*This Agreement commenced on the Commencement Date and continues until 30 June 2024 unless earlier terminated in accordance with clause 3.2 or clause 14. The Term may be extended by mutual agreement of the parties.*”

44.AMENDMENT

44.1.All references to “Agreement”, “hereunder”, “herein”, “hereof” or similar words referring to the

Consultancy Agreement, from and after the Amendment Effective Date, shall mean and refer to the Consultancy Agreement as amended by this Amendment No.3.

45.COUNTERPARTS

45.1.This Amendment No.3 may be executed in any number of counterparts, and by the Parties on separate counterparts, each of which when so executed will constitute an original but all of which together will evidence the same agreement.

IN WITNESS whereof this Amendment No.3 has been entered into on the date first herein written.

SIGNED on behalf of the Company:

/s/ Corey Fishman

…..
Signature

Name: Corey Fishman

Title: Director

SIGNED By Contractor:

/s/ Michael Dunne

…..
Signature

Name: Michael Dunne

SCHEDULE 5

AMENDMENT NO.4

Dated August 9, 2024

ITERUM THERAPEUTICS INTERNATIONAL LIMITED

-and-

MICHAEL DUNNE

AMENDMENT TO CONTRACT FOR SERVICES

THIS AMENDMENT to a CONTRACT FOR SERVICES is made and entered into on August 9, 2024, by and between:

(1) **ITERUM THERAPEUTICS INTERNATIONAL LIMITED** whose registered office is at Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, D02 YW24, Ireland (the **Company**); and

(2) **MICHAEL DUNNE** of 30 Cromwell Place, Old Saybrook, CT, 06475 (the **Contractor**),

ereinafter referred to as **Amendment No.4**.

The Company and the Contractor are hereinafter individually referred to as a **Party** or collectively referred to as the **Parties**.

RECITALS

K.The Parties entered into a Contract for Services dated May 25, 2022, pursuant to which the Contractor agreed to provide the Services to the Company and any Associated Company upon and subject to the terms and conditions therein contained (the **Consultancy Agreement**), a copy of which is attached hereto in Schedule 1.

L.The Parties entered into an Amendment Agreement dated December 31, 2022, pursuant to which the Parties agreed to extend the Term of the Consultancy Agreement until June 30, 2023, upon and subject to the terms and conditions therein contained (**Amendment No.1**), a copy of which is attached hereto in Schedule 2.

M.The Parties entered into an Amendment Agreement dated June 15, 2023, pursuant to which the Parties agreed to extend the Term of the Consultancy Agreement until December 31, 2023, upon and subject to the terms and conditions therein contained (**Amendment No.2**), a copy of which is attached hereto in Schedule 3.

N.The Parties entered into an Amendment Agreement dated June 15, 2023, pursuant to which the Parties agreed to extend the Term of the Consultancy Agreement until June 30, 2024, upon and subject to the terms and conditions therein contained (**Amendment No.3**), a copy of which is attached hereto in Schedule 4.

O.The Parties hereto wish to further amend the Consultancy Agreement as prescribed herein, effective as of June 30, 2024 (the **Amendment Effective Date**).

IT IS HEREBY AGREED as follows:

46.EXISTING TERMS, CONDITIONS AND DEFINITIONS

46.1.Unless specifically amended herein, the terms and conditions described in the Consultancy Agreement shall remain in full force and effect.

46.2.Capitalised terms (including those used in the Recitals above) shall be as defined in the Consultancy Agreement, Amendment No.1, Amendment No.2 and Amendment No.3.

47.TERM

47.1.Clause 3.1 (“Term”) of the Consultancy Agreement shall be amended to read as follows:

"*This Agreement commenced on the Commencement Date and continues until 31 December 2024 unless earlier terminated in accordance with clause 3.2 or clause 14. The Term may be extended by mutual agreement of the parties.*"

48.AMENDMENT

48.1.All references to "Agreement", "hereunder", "herein", "hereof" or similar words referring to the Consultancy Agreement, from and after the Amendment Effective Date, shall mean and refer to the Consultancy Agreement as amended by this Amendment No.4.

49.COUNTERPARTS

49.1.This Amendment No.4 may be executed in any number of counterparts, and by the Parties on separate counterparts, each of which when so executed will constitute an original but all of which together will evidence the same agreement.

IN WITNESS whereof this Amendment No.4 has been entered into on the date first herein written.

SIGNED on behalf of the Company:

/s/ Corey Fishman

…..
Signature

Name: Corey Fishman

Title: Director

SIGNED By Contractor:

/s/ Michael Dunne

…..
Signature

Name: Michael Dunne

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statements Nos. 333-257322, 333-261558, 333-225236, 333-230496, 333-237198, and 333-245655 on Form S-8 and No. 333-267795 on Form S-3 of our report dated February 7, 2025, with respect to the consolidated financial statements of Iterum Therapeutics plc.

/s/ KPMG

Dublin, Ireland
February 7, 2025

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Corey Fishman, certify that:

1.I have reviewed this Annual Report on Form 10-K of Iterum Therapeutics plc;

2.Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3.Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4.The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a)Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b)Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c)Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d)Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5.The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a)All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b)Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 7, 2025

By: /s/ Corey Fishman
Corey Fishman
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Judith Matthews, certify that:

1.I have reviewed this Annual Report on Form 10-K of Iterum Therapeutics plc;

2.Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3.Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4.The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a)Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b)Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c)Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d)Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5.The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a)All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b)Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 7, 2025

By: /s/ Judith Matthews
Judith Matthews
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Iterum Therapeutics plc (the "Company") for the year ended December 31, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Corey Fishman, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to his knowledge on the date hereof:

(1)The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2)The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 7, 2025

By: /s/ Corey Fishman
Corey Fishman
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Iterum Therapeutics plc (the "Company") for the year ended December 31, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Judith Matthews, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to her knowledge on the date hereof:

(1)The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2)The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 7, 2025

By: /s/ Judith Matthews
Judith Matthews
Chief Financial Officer
(Principal Financial and Accounting Officer)