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, 2023

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.)**

Fitzwilliam Court, 1st Floor,
Leeson Close,
Dublin 2, Ireland
(Address of principal executive offices)

Not applicable
(Zip Code)

(+353) 1 669-4820
(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, 2023, the last business day of the Registrant's most recently completed second fiscal quarter was $13.7 million.

The number of shares of Registrant's ordinary shares outstanding as of February 29, 2024 was 16,426,784.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates by reference information from the definitive proxy statement for the Registrant's 2024 Annual Meeting of Shareholders, which is expected to be filed with the Securities and Exchange Commission not later than 120 days after the Registrant's fiscal year ended December 31, 2023.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

- our use of cash reserves;
- 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 resolve the issues set forth in the Complete Response Letter (CRL) received from the U.S. Food and Drug Administration in July 2021 in connection with our New Drug Application (NDA) for oral sulopenem and resubmit our NDA;
- 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, including with respect to the potential resubmission of our NDA for oral sulopenem;
- the commercialization of our product candidates, if approved;
- our manufacturing plans;
- our sales, marketing and distribution capabilities and strategy;
- market acceptance of any product we successfully commercialize;
- the pricing, coverage and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates 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; and
- our strategic process to sell, license, or otherwise dispose of our rights to oral sulopenem to maximise 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.

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 (SEC) as exhibits to this Annual Report with the understanding that our actual future results, levels of activity, performance, and events and circumstances may be materially different from what we expect.

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

- We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of December 31, 2023, we had $23.9 million of cash, cash equivalents and short-term investments. Based on our available cash resources, including amounts raised subsequent to the year end under the "at-the-market" agreement, as disclosed in Note 17 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we do not believe that our existing cash, cash equivalents and short-term investments 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 including through repayment of the 6.500% Exchangeable Senior Subordinated Notes due in January 2025 (Exchangeable Notes).
- We will require additional capital to fund our operations and may be unable to obtain financing when needed or on acceptable terms. Additionally, in the event we are not able to obtain shareholder approval for the disapplication of pre-emption rights over our ordinary shares at a general meeting of the shareholders, our ability to raise additional capital through the issue of new shares for cash will be severely limited. Additional capital will also be required in order to repay the Exchangeable Notes when they become due. We may not have enough available cash or be able to obtain financing at that time. Our failure to make repayments when due would constitute a default under the indenture governing the Exchangeable Notes. A default under that indenture could also lead to a default under any agreements governing our future indebtedness.
- 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, 2023, we had an accumulated deficit of $461.3 million.
- In July 2021, we received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration (FDA) regarding our new drug application ("NDA") for oral sulopenem for the treatment of uncomplicated urinary tract infections (uUTIs) in patients with a quinolone non-susceptible pathogen. In the CRL, the FDA determined that additional data are necessary to support approval for the treatment of adult women with uUTIs caused by designated susceptible microorganisms proven or strongly suspected to be non-susceptible to a quinolone. The FDA 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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024). There can be no assurance that we will be in a position to resolve the matters set forth in the CRL or that the data generated by the REASSURE clinical trial and/or the additional PK/PD data will be adequate to support resubmission or approval of our NDA.
- We are heavily dependent on the success of our sulopenem program, and our ability to develop, obtain marketing approval for and successfully commercialize oral sulopenem and sulopenem. If we are unable to obtain marketing approvals for oral sulopenem or sulopenem, or if thereafter we fail to commercialize oral sulopenem or sulopenem or experience significant delays in doing so, our business will be materially harmed.
- Our company has no experience in obtaining regulatory approval for a drug. If clinical trials of oral sulopenem, sulopenem or any other product candidate that we may advance to clinical trials fail to demonstrate safety and efficacy to the satisfaction of the FDA or comparable foreign regulatory authorities, or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of oral sulopenem, sulopenem or any other product candidate.
- Serious adverse events or undesirable side effects or other unexpected properties of oral sulopenem, sulopenem or any other product candidate may be identified during development or after approval that could delay, prevent or cause the withdrawal

of regulatory approval, limit the commercial potential, or result in significant negative consequences following marketing approval.

- Even if a product candidate does obtain regulatory approval, it may never achieve the market acceptance by physicians, patients, hospitals, third-party payors and others in the medical community that is necessary for commercial success, and the market opportunity may be smaller than we estimate.
- 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., sulopenem or any other product candidate may not be successfully commercialized, if such product candidate is approved.
- Our exploration and pursuit of strategic alternatives may not be successful.
- We cannot predict whether bacteria may develop resistance to oral sulopenem or sulopenem, which could affect their revenue potential.
- We contract with third parties for the manufacture of preclinical and clinical supplies and expect to continue to do so in connection with any future commercialization and for any future clinical trials and commercialization of our product candidates and potential product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- We rely heavily on the exclusive license agreement with Pfizer Inc., or Pfizer, for the patent rights and know-how required to develop and commercialize sulopenem etzadroxil 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 oral sulopenem or our other technology and product candidates, or if the scope of the patent protection or intellectual property rights we obtain is not sufficiently broad, we may not be able to successfully develop or commercialize oral sulopenem or any other product candidates or technology or otherwise compete effectively in our markets.
- The volatility of our shares and shareholder base may hinder or prevent us from engaging in beneficial corporate initiatives. As our shareholder base is comprised of a large number of retail (or non-institutional) investors, this 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. Failure to secure sufficient votes on a particular matter 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. For example, we asked our shareholders to approve the disapplication of statutory pre-emption rights over the increased authorized share capital that was approved by our shareholders at our annual general meeting of shareholders in May 2023 (the 2023 Annual Meeting). However, we did not receive the affirmative vote of at least 75% of the votes cast as required under Irish law for the passing of such resolutions at the 2023 Annual Meeting or at subsequent extraordinary general meetings of shareholders held in August 2023 and January 2024. As a result, our ability to raise additional capital to finance our business through the issue of new shares for cash is severely limited.

PART I

Item 1. Business.

Overview

We are a clinical-stage pharmaceutical company dedicated to developing and commercializing sulopenem to be potentially the first oral penem available in the United States and the first and only oral and intravenous (IV) branded penem available globally. Penems, including thiopenems and carbapenems, belong to a class of antibiotics more broadly defined as ß-lactam antibiotics, the original example of which was penicillin, but which now also includes cephalosporins. Sulopenem is a potent, thiopenem antibiotic delivered intravenously which is active against bacteria that belong to the group of organisms known as gram-negatives and cause urinary tract and intra-abdominal infections. We have also successfully developed sulopenem in an oral tablet formulation, sulopenem etzadroxil-probenecid, which we refer to as oral sulopenem. We believe that sulopenem and oral sulopenem have the potential to be important new treatment alternatives to address growing concerns related to antibacterial resistance without the known toxicities of some of the most widely used antibiotics, specifically fluoroquinolones.

During the third quarter of 2018, we initiated three clinical trials in our Phase 3 development program which included: a Phase 3 uncomplicated urinary tract infection (uUTI) clinical trial, known as Sulopenem for Resistant Enterobacteriaceae (SURE) 1, comparing oral sulopenem to oral ciprofloxacin in women with uUTI, a Phase 3 complicated urinary tract infection (cUTI) clinical trial known as SURE 2, comparing IV sulopenem followed by oral sulopenem to IV ertapenem followed by oral ciprofloxacin in adults with cUTI and a Phase 3 complicated intra-abdominal infection (cIAI) clinical trial known as SURE 3, comparing IV sulopenem followed by oral sulopenem to IV ertapenem followed by a combination of oral ciprofloxacin and oral metronidazole in adults with cIAI. We designed one Phase 3 clinical trial in each indication based on our end of Phase 2 meeting with the U.S. Food and Drug Administration (FDA) and feedback from the European Medicines Agency (EMA). We conducted the Phase 3 clinical trials under Special Protocol Assessment (SPA) agreements from the FDA. 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 (SURE 3). 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-New Drug Application (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 SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REnewed ASsessment of Sulopenem in uUTI caused by Resistant Enterobacterales (REASSURE), in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024). 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 shareholder value. In connection with this strategic process, we have engaged a financial advisor to assist management and the board in evaluating strategic alternatives.

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

The treatment of urinary tract and intra-abdominal infections has become more challenging because of the development of resistance by pathogens responsible for these diseases. There are approximately 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. Elevated risk patients were defined in the research as patients with recurrent UTIs, elderly patients, patients who have a suspected or confirmed drug-resistant infection, patients with comorbidities (e.g., Diabetes mellitus) or that are immunocompromised, patients that have had a recent hospitalization, patients with a history of prior antibiotic failure and patients in a long-term care setting. Treatment failures pose significant clinical and economic challenges to the healthcare system. 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.

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

None of the most commonly used oral antibiotics for treatment of uUTIs were initially approved by the FDA within the last two decades. We believe oral sulopenem will be an important treatment option for elevated risk uUTI patients because of its potency against resistant pathogens, as well as its spectrum of antibacterial activity. In addition, oral sulopenem will allow patients who develop an infection with a resistant pathogen but are stable enough to be treated in the community, to avoid the need for an IV catheter and even hospitalization.

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

If approved, and in the event our strategic process to sell, license, or otherwise dispose of our rights to oral sulopenem to maximise value for our stakeholders, does not result in any type of transaction, we would plan to commercialize our sulopenem program in the United States with a commercial partner and/or on our own with a targeted sales force in the community setting. Data from an ongoing epidemiology study to quantify quinolone resistance by zip code, in addition to data from our clinical trials and available prescriber data, would inform our initial targeted sales force as to where the medical need for a new, effective therapy for

UTIs is highest in the community setting. Outside of the United States, we are evaluating our options to maximize the value of our sulopenem program.

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

As of February 29, 2024, 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 also own two 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, and the other U.S. patent directed to the method of use of oral sulopenem in treating multiple diseases, including uUTIs. The patents owned by us are scheduled to expire no earlier than 2039, excluding any additional term for patent adjustments or patent term extensions. We also own three pending U.S. patent applications, and twenty four pending foreign patent applications, which collectively cover uses of sulopenem and probenecid and bilayer tablets of sulopenem etzadroxil and probenecid. 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, the FDA has designated sulopenem and oral sulopenem as Qualified Infectious Disease Products (QIDP) for the indications of uUTI, cUTI, cIAI, community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease pursuant to the Generating Antibiotic Incentives Now Act (the GAIN Act). Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. QIDP status makes sulopenem and oral sulopenem eligible to benefit from certain incentives for the development of new antibiotics provided under the GAIN Act. Further, QIDP status could add five years to any regulatory exclusivity period that we may be granted. QIDP status for other indications is also possible given the coverage of gram-negative and gram-positive bacteria by sulopenem, pending submission of additional documentation and acceptance by the FDA. Fast track status provides an opportunity for more frequent meetings with the FDA, more frequent written communication related to the clinical trials, eligibility for accelerated approval and priority review and the potential for a rolling review. None of our licensed patents cover the IV formulation of sulopenem.

Sulopenem Program, Clinical and Regulatory Status

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

During the third quarter of 2018, we initiated three clinical trials in our Phase 3 development program, being the SURE 1 trial, the SURE 2 trial and the SURE 3 trial. We designed one Phase 3 clinical trial in each indication based on our end of Phase 2 meeting with the FDA and feedback from the EMA. We conducted the Phase 3 clinical trials under SPA agreements from the FDA. 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 (SURE 3). 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 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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024).

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. We are now focused on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing stakeholder value and have 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 its rights to sulopenem. Pending the outcome of such strategic process, the key elements of our strategy continue to include the following:

- ***Obtain regulatory approval for oral sulopenem in the United States*.** Resubmit our NDA to the FDA for oral sulopenem which is expected in the second quarter of 2024.
- ***Consider regulatory strategy outside the United States.*** We are considering the timing of a potential submission of a Marketing Authorization Application (MAA) to the EMA.

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, our strategy may include some or all of the following elements:

- ***Maximize commercial potential of our sulopenem program.*** If approved by the FDA, we may seek a commercial partner and/or directly commercialize oral sulopenem 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.
- ***Pursue the development of oral sulopenem and sulopenem in additional indications***. In the future, we may also pursue development of our sulopenem program in additional indications in adults and children, including cUTIs, community acquired bacterial pneumonia, non-tuberculous mycobacterial pulmonary disease, 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.

The Medical Need

Urinary Tract and Intra-Abdominal Infections

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

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

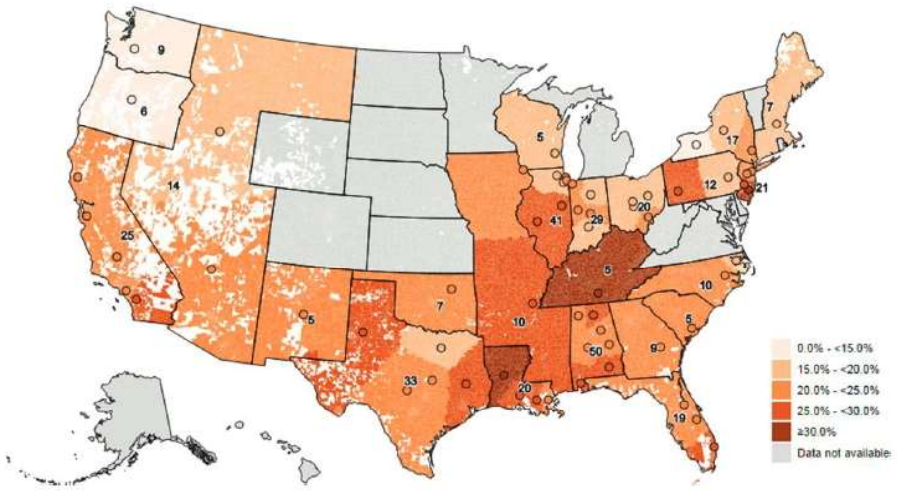
Antimicrobial Resistance is Increasing

E. coli is growing increasingly resistant to many classes of antibiotics, which is especially problematic for patients suffering from UTIs because *E. coli* is the primary cause of those infections. The market-leading antibiotics, fluoroquinolones (e.g., Cipro,

Levaquin) and trimethoprim-sulfamethoxazole (e.g., Bactrim, Septra), currently have *E. coli* resistance rates over 20% nationally. In 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% (EU/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-sulphamethoxazole, 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

There are approximately 15 million emergency room and office visits for symptoms of 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 consequences associated with treatment failure. Elevated risk patients were defined in the research as patients with recurrent UTIs, elderly patients, patients who have a suspected or confirmed drug-resistant infection, patients with comorbidities (e.g., Diabetes mellitus) or that are immunocompromised, patients that have had a recent hospitalization, patients with a history of prior antibiotic failure and patients in a long-term care setting.

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

Limited Treatment Options

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

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

The Challenge of Developing Antibiotics

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

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

continue to need new antibiotics that stay one step ahead of these mutating bacteria in order to protect against the infections that they cause.

The Solution to Rising Resistance

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

These new agents will need to:

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

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

Our Sulopenem Program

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

Potential Advantages of Oral Sulopenem and Sulopenem

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

Sulopenem's differentiating characteristics include:

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

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

- ***Documented safety and tolerability profile.*** In our completed Phase 3 program, sulopenem IV and oral sulopenem 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 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 (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 recently completed uUTI trial, REASSURE, patients received either oral sulopenem or Augmentin®. Among 2,214 treated patients, treatment related adverse events were observed in 18.9% and 12.3% of patients on sulopenem 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 sulopenem 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 sulopenem and 0.4% of patients on Augmentin®. Serious adverse events were seen in 0.0% of patients on sulopenem 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, if approved, offer both important formulations as therapeutic options.
- ***Advanced manufacturing program.*** The synthetic pathway for sulopenem, initially defined in the 1980s, has now evolved through its third iteration, incorporating improvements in yield and scalability. We plan to register two different contract manufacturing organizations to manufacture the API for oral sulopenem. One manufacturer has completed process validation for oral sulopenem to date providing sufficient API for clinical supplies and commercial launch if oral sulopenem is approved for marketing. We will initially rely on a single third-party facility to manufacture all of our sulopenem tablets. In the future, given the importance of sulopenem to our potential commercial results, we will consider establishing additional sources.

Market Opportunity for Oral Sulopenem and Sulopenem

Based upon the clinical evidence to date in eradicating key pathogens, coupled with unmet medical need, if approved, we expect the commercial opportunity for oral sulopenem 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 oral sulopenem's value proposition will aid physicians in the community setting to address the unmet need for a safe and effective oral uUTI therapy to treat the growing number of patients with suspected or confirmed resistant pathogen(s). In addition, we believe our sulopenem program will offer a compelling value proposition to hospitals by enabling the transition of patients from IV therapy in the inpatient setting to an oral therapy in the community.

Oral Sulopenem and Sulopenem Clinical Development Program

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

Both sulopenem and oral sulopenem have received QIDP designation status for the indications of uUTI, cUTI and cIAI as well as for community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. QIDP designation status for other indications is also possible given the coverage of gram-negative and gram-positive bacteria by sulopenem, pending submission of additional documentation and acceptance by the FDA. We 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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024).

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 $\geq$ 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.

Penem Class:	*E. coli* N = 983		*K. pneumoniae* N = 273		*P. mirabilis* N = 91	
	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. As such, susceptibility breakpoints have not yet been determined for sulopenem.

Animal Models

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

Non-clinical Pharmacology

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

Phase 1 Program

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

Protocol	Year	Dose (mg), other medication	Subjects on sulopenem or sulopenem etzadroxil	Treatment (Days)
Sulopenem (CP-70,429)—Phase 1 Single Dose Clinical Trials				
A109001	1987	1000 mg	6	1
Japanese PK		250 mg, 500 mg, 1000 mg	18	1
A7371007	2007	400 mg, 800 mg, 1600 mg, 2400 mg, 2800 mg, placebo	24	1
IT001-105	2018	366 mg IV	34	1
Sulopenem (CP-70,429)—Phase 1 Multiple Dose Clinical Trials				
Japanese PK		500 mg, 1000 mg	12	5
Japanese PK		1000 mg	6	5
A1091001	2009	800 mg, 1200 mg, 1600 mg, 2000 mg, placebo	40	14
IT001-103	2019	1000 mg	15	2
IT001-104	2019	1000 mg	10	3

Protocol	Year	Dose (mg), other medication	Subjects on sulopenem or sulopenem etzadroxil	Treatment (Days)
IT001-105	2018	1000 mg	12	3
Sulopenem etzadroxil (PF-03709270)—Phase 1 Single Dose Clinical Trials				
A8811001	2007	400 mg, 600 mg, 1000 mg, 2000 mg, placebo	9	1
A8811006	2008	2000 mg	4	1
A8811007	2007	600 mg, probenecid	4	1
A8811008	2008	1200 mg, probenecid	24	1
A8811018	2008	1000 mg, 1200 mg, probenecid, aluminum hydroxide, pantoprazole	17	1
A8811003	2008	2000 mg, 4000 mg, 6000 mg, 8000 mg, placebo	11	1
IT001-101	2017	500 mg, 1000 mg, probenecid	48	1
IT001-102	2017	500 mg, probenecid	13	1
Sulopenem etzadroxil (PF-03709270)—Phase 1 Multiple Dose Clinical Trials				
A8811003	2008	2000 mg, 1200 mg, probenecid, placebo	18	10
A8811015	2009	500 mg, 1000 mg, 1500 mg, probenecid, placebo, Augmentin	48	7
IT001-101	2017	500 mg, probenecid	64	7
IT001-103	2019	Bilayer tablet, 500 mg	47	2
IT001-104	2019	Bilayer tablet, 500 mg	19	3
IT001-105	2018	500 mg, bilayer tablet	34	2
Sulopenem (CP-70,429), Sulopenem etzadroxil (PF-03709270)—Phase 1 Renal Impairment Clinical Trial				
A8811009	2010	200mg, 800 mg sulopenem or 1000 mg sulopenem etzadroxil	29	1
		Total	566	

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

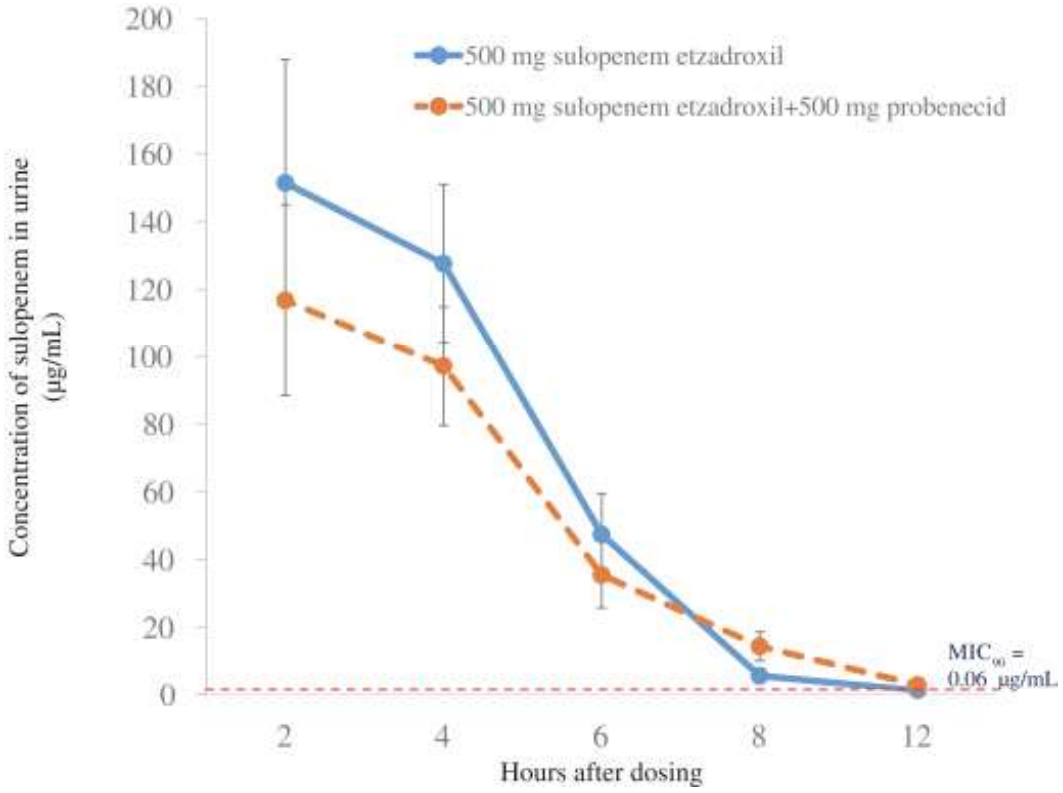
Oral Sulopenem

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

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

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

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



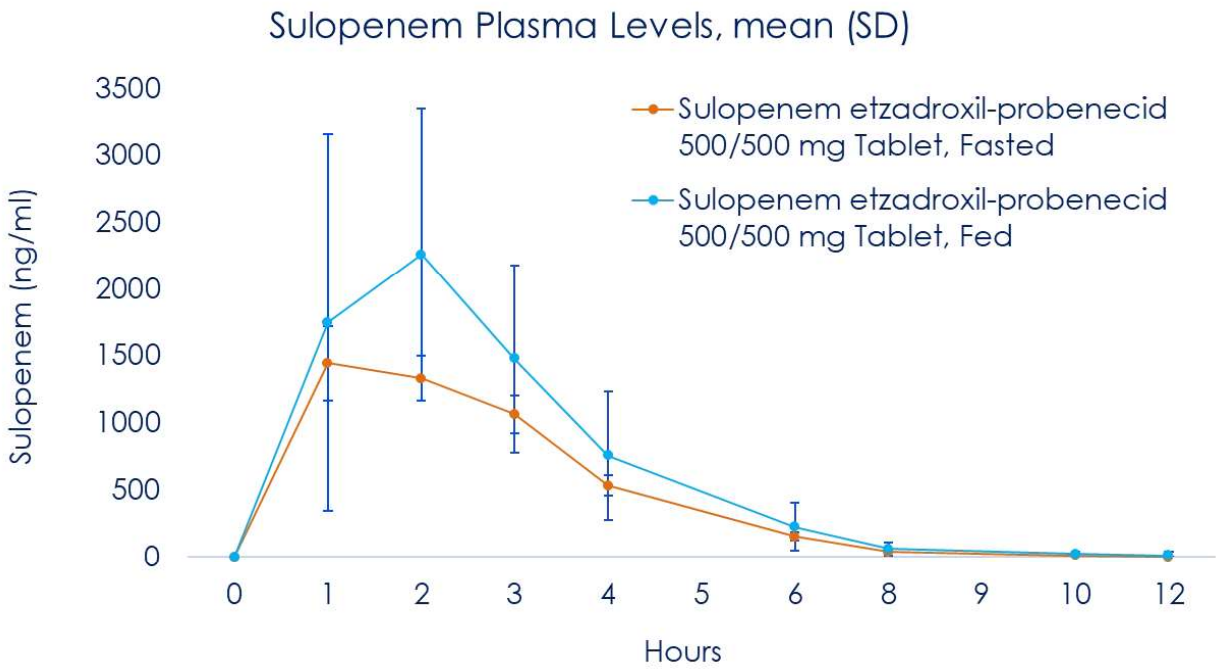
In IT001-102, we evaluated sulopenem etzadroxil administered with and without probenecid in a randomized cross-over trial in healthy volunteers in a fasted state. Subjects receiving sulopenem etzadroxil in a powder-in-a-bottle formulation co-administered with a separate tablet of probenecid demonstrated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

			Sulopenem Parameter (Day 1)			
Treatment	**N**	**Descriptive Statistic**	**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; $AUC_{0-\infty}$ = area under the curve from the initiation of dosing extrapolated through infinite time

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

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

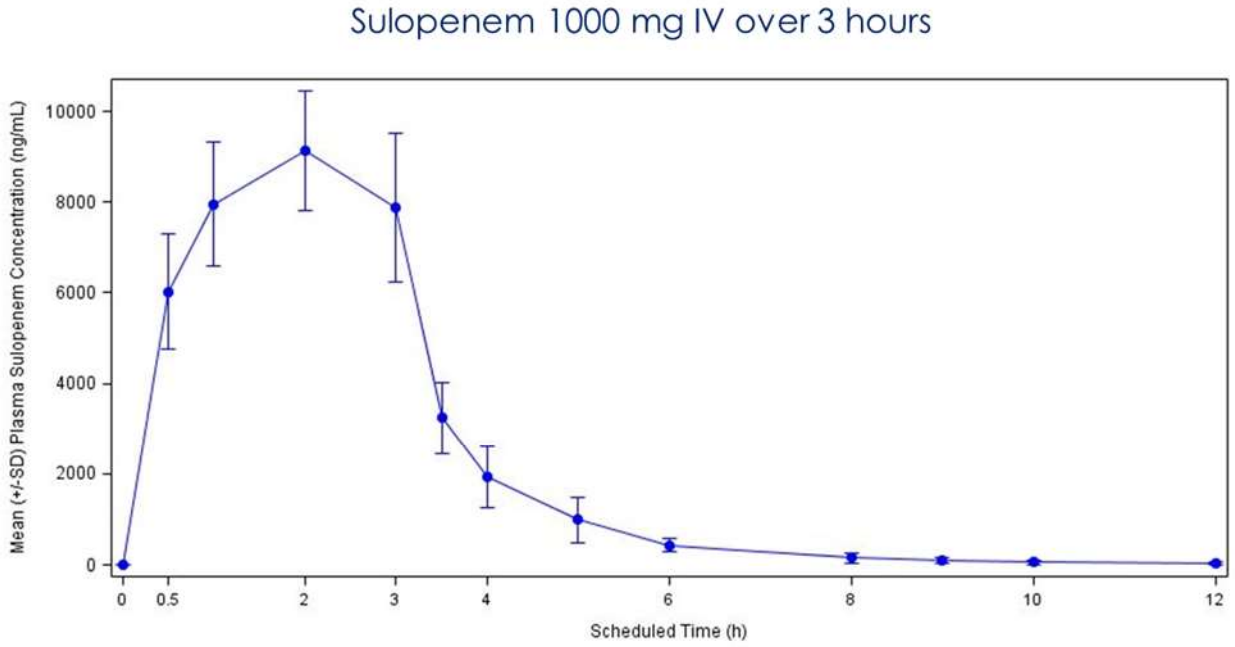
Doses of sulopenem up to 2800 mg as a single IV dose and 2000 mg BID, or twice daily, of sulopenem as IV over fourteen days were studied in three Phase 1 clinical trials in healthy adults, one study in patients with renal insufficiency in the United States and two Phase 1 clinical trials in Japan. Results 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	.15 9	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

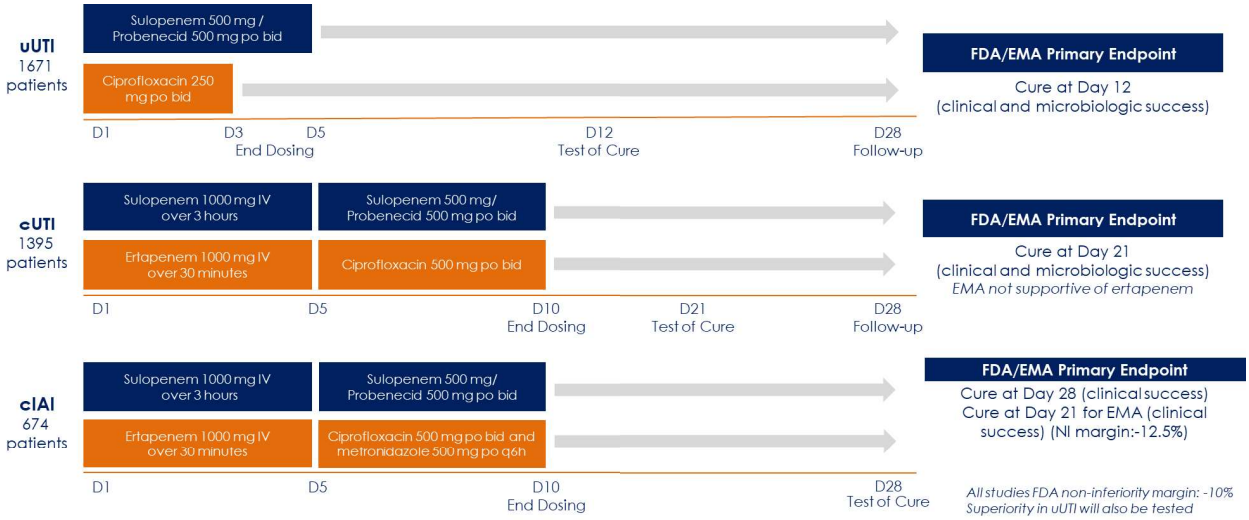
In 2009, Pfizer initiated a Phase 2, randomized, double-blind, double-dummy clinical trial in hospitalized patients with CAP comparing two regimens of IV sulopenem followed by sulopenem etzadroxil to ceftriaxone IV followed by amoxicillin-clavulanate. The sulopenem regimens were a single 600 mg IV dose 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 - Completed

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, 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, 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)

Safety Profile of Oral Sulopenem and Sulopenem

Sulopenem is a thiopenem and a member of the class of ß-lactam antibiotics, a class from which numerous safe and well tolerated antibiotics have been available for over thirty years.

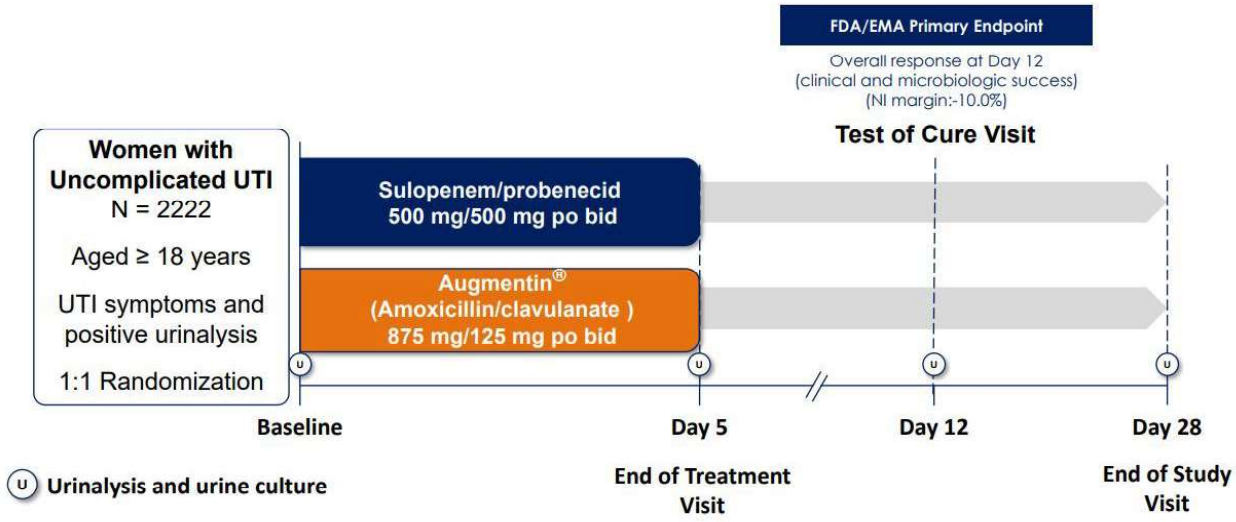
In the cIAI trial, among 668 treated patients, treatment-related adverse events were observed in 6.0% and 5.1% of patients on sulopenem and ertapenem, respectively, with the most commonly reported drug-related adverse event being diarrhea, which was observed in 4.5% and 2.4% of patients on sulopenem 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 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 (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 recently completed uUTI trial, REASSURE, patients received either oral sulopenem or Augmentin®. Among 2,214 treated patients, treatment related adverse events were observed in 18.9% and 12.3% of patients on sulopenem 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 sulopenem 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 sulopenem and 0.4% of patients on Augmentin®. Serious adverse events were seen in 0.0% of patients on sulopenem and 0.5% of patients on Augmentin® with no drug-related serious adverse event.

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

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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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%. We expect to resubmit our NDA to the FDA in the second quarter of 2024.

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

	Sulopenem/probenecid 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

Pfizer License Agreement

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

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

Under the Pfizer License, we have paid Pfizer a one-time nonrefundable upfront fee of $5.0 million and a total of $15.0 million in clinical milestones based on first patient dosed in our Phase 3 clinical trials with sulopenem etzadroxil and sulopenem IV and are obligated to pay Pfizer potential future regulatory milestone payments, as well as potential sales milestones upon achievement of net sales ranging from $250.0 million to $1.0 billion for each product type (sulopenem etzadroxil and other prodrugs, and sulopenem and other non-prodrugs). We are obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage of marginal net sales of each licensed product. Pfizer also received 381,922 of our Series A preferred shares (which converted to 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 two 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, and the other U.S. patent directed to the method of use of oral sulopenem in treating multiple diseases, including uUTIs. We also own three pending U.S. patent applications, and twenty four pending foreign patent applications, which collectively cover uses of sulopenem and probenecid and bilayer tablets of sulopenem etzadroxil and probenecid. 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 February 29, 2024, 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 also own two 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, and the other U.S. patent directed to the method of use of oral sulopenem in treating multiple diseases, including uUTIs. The patents owned by us are scheduled to expire no earlier than 2039, excluding any additional term for patent adjustments or patent term extensions. We also own three 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. 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 oral sulopenem and sulopenem, if approved, will be efficacy, coverage of drug-resistant strains of bacteria, safety and tolerability profile, reliability, convenience of oral dosing, price, availability of reimbursement from governmental and other third-party payors and susceptibility to drug resistance.

If approved, oral sulopenem could compete with a few oral antibiotics currently in late-stage clinical development to treat uUTIs, including gepotidacin from GlaxoSmithKline and pivmecillinam from Utility Therapeutics Limited. If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

We also expect that oral sulopenem, if approved, would compete with future and current generic versions of marketed oral antibiotics such as levofloxacin, ciprofloxacin, nitrofurantoin, fosfomycin, amoxicillin-clavulanate, cephalexin and trimethoprim-sulfamethoxazole. If approved, we believe that oral sulopenem would compete effectively against these compounds on the basis of sulopenem's potential:

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

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, Xerava from Innoviva, 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 oral sulopenem;
- has a convenient once a day dosing over a three-hour infusion period;
- has a broad spectrum activity against a wide variety of resistant and MDR gram-negative bacteria;
- has a low probability of drug resistance; and
- has a favorable safety and tolerability profile.

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. 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 European Union (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, 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.

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 and securing FDA review and approval of the NDA; and
- commitment to comply with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy (REMS) and the potential requirement to conduct post-approval studies.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. Preclinical tests intended for submission to the FDA to support the safety of a product candidate must be conducted in compliance with GLP regulations and the United States Department of Agriculture's Animal Welfare Act. A drug sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Such studies are typically referred to as IND-enabling studies. Some preclinical testing may continue even after the IND is submitted.

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 safety monitoring board (DSMB) or 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 DSMB or DMC maintains access. Suspension or termination of development during any phase of a clinical trial can occur if the DSMB or 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 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 January 2024, the FDA issued draft guidance setting out its policies for the collection of race and ethnicity data in clinical trials.

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.

Sponsors of clinical trials 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. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although the FDA has historically not enforced these reporting requirements due to the long delay of the U.S. Department of Health and Human Services, or HHS, the FDA has issued several pre-notices for voluntary corrective action and several notices of non-compliance during the past two years. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinicaltrials.gov, as required, 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.

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.

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. Our Expanded Access Program for oral sulopenem for the treatment of cUTIs due to quinolone non-susceptible uropathogens after an initial course of effective intravenous therapy became available in December 2020.

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 2024 is $4,048,695 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2024 is $416,734. Under the Prescription Drug User Fee Act (PDUFA) guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. 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.

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 that offer major advances in treatment for a serious condition or provide a treatment where no adequate therapy exists. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. These six and ten month review periods are

measured from the "filing" date for NDAs for new molecular entities. The FDA will automatically give a priority review designation for the first application submitted in respect of a product for which a QIDP designation was granted.

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.

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.

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

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

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

In addition, the distribution of prescription pharmaceutical products is subject to 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 in place but, in August 2023, the FDA set a one-year period in which it would exercise its enforcement discretion with respect to these requirements.

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. This extension is in addition to any pediatric exclusivity extension awarded, and the extension will be awarded only to a drug first approved on or after the date of enactment.

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

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of 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 HIPAA, the 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, eleven 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.

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.

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.

Marketing Authorization

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure is compulsory for medicinal products produced by biotechnology or those medicinal products containing new active substances for specific indications such as the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and designated orphan medicines, and optional for other medicines which are highly innovative. Under the centralized procedure, a marketing application is submitted to the EMA where it will be evaluated by the Committee for Medicinal Products for Human Use and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all European Union member states within 67 days of receipt of the opinion. The initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period. The decentralized procedure provides for approval by one or more "concerned" member states based on an assessment of an application performed by one member state, known as the "reference" member state. Under the decentralized approval procedure, 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.

Conditional approval

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) a marketing authorization may be granted prior to submission of comprehensive clinical data provided that 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.

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.

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 United Kingdom's withdrawal from the European Union took place on January 31, 2020. The European Union and the United Kingdom reached an agreement on their new partnership in the Trade and Cooperation Agreement (Agreement), which was applied provisionally beginning on January 1, 2021 and which entered into force on May 1, 2021. The Agreement focuses primarily on free trade by ensuring no tariffs or quotas on trade in goods, including healthcare products such as medicinal products. Thereafter, the European Union and the United Kingdom will form two separate markets governed by two distinct regulatory and legal regimes. As such, the Agreement seeks to minimize barriers to trade in goods while accepting that border checks will become inevitable as a consequence that the United Kingdom is no longer part of the single market. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency (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.

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 European Economic Area (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 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.-UK "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.-UK 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; the federal Health Insurance Portability and Accountability Act of 1996 (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, or the 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.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new executive order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this executive order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

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, or 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, or 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. Nine states (Colorado, Florida, Maine, New Hampshire, New Mexico, North Dakota, Texas, Vermont and Wisconsin) have passed laws allowing for the importation of drugs from Canada. Certain of these states have submitted Section 804 Importation Program proposals and are awaiting FDA approval. On January 5, 2023, the FDA approved Florida's plan for Canadian drug importation.

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, or IRA, further delayed implementation of this rule to January 1, 2032.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. To address these costs, the executive order directs the HHS to create a plan within 45 days to combat "excessive pricing of prescription drugs and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such drugs, and to address the recurrent problem of price gouging." Thereafter, on September 9, 2021, HHS released its plan to reduce drug prices. The key features of that plan are to: (a) make drug prices more affordable and equitable for all consumers and throughout the health care system by supporting drug price negotiations with manufacturers; (b) improve and promote competition throughout the prescription drug industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

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.

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. 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 shareholder value. In connection with this strategic process, we have engaged a financial advisor to assist management and the board in evaluating strategic alternatives.

Given our stage of development, we have not yet established a commercial organization or distribution capabilities for our initial indication. 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 our sulopenem program in the United States with a commercial partner and/or on our own with a targeted sales force in the community setting.

Prior to receiving marketing approval, and subject to the outcome of our strategic process, we may 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, prior to approval, and subject to the outcome of our strategic process, we may 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. Some pre-commercialization activities including research and planning were undertaken in early 2021 which can be built on if and when we are in a position to resume commercialization activities.

If the FDA approves oral sulopenem, subject to the outcome of our strategic process, we may build a commercial infrastructure to launch oral sulopenem in the United States. We would plan that the 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 would also plan to have in place a patient and healthcare practitioner support group to assist with information requests, reimbursement logistics and assistance, and provide educational materials where appropriate.

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 oral sulopenem, 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 sulopenem's 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 may 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 currently rely 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. As of February 29, 2024, 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 intend to have a third-party manufacturer produce the oral sulopenem bilayer tablets. In the future, given the importance of our oral formulation, we plan to pursue additional sources to manufacture tablets.

Employees and Human Capital

As of February 29, 2024, we had 14 full-time employees, including a total of three 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. Eight of our employees were primarily engaged in research and development activities, with the rest providing administrative, business and operations support. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our employee relations to be good. We may need to increase our workforce to support additional clinical 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 principal executive offices are located at Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, D02 YW24, Ireland, and our telephone number is (+353) 1 669-4820.

Available Information

We maintain a website with the address www.iterumtx.com. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934 (the Exchange Act). We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. You can review our electronically filed reports, proxy and information statements and other information that we file with the SEC on the SEC's web site at http://www.sec.gov. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% 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, or SEC, in evaluating our company and our business. Investing in our ordinary shares involves a high degree of risk. If any of the events described in the following Risk Factors and the risks described elsewhere in this Annual Report on Form 10-K actually occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our ordinary shares could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Position and Capital Requirements

We have 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 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, 2023, we had $23.9 million of cash, cash equivalents and short-term investments. Based on our available cash resources, including amounts raised subsequent to the year end under the "at-the-market" agreement, as disclosed in Note 17 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we do not believe that our existing cash, cash equivalents and short-term investments 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 including through repayment of the 6.500% Exchangeable Senior Subordinated Notes due in January 2025 (Exchangeable Notes).

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 of 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 addition, our ability to raise additional capital through the issue of new shares for cash is limited to issuing only 1.8 million ordinary shares (or rights to acquire such shares) for cash, based on the amount of authorized ordinary shares unissued or unreserved and free from any statutory rights of pre-emption, and therefore available for issuance as of February 29, 2024. While shareholders approved an increase of an additional 60,000,000 ordinary shares at our annual general meeting in May 2023 (the "Additional Shares"), we did not receive approval for the disapplication of statutory pre-emption rights over such shares. Absent shareholder approval of the dis-application of statutory pre-emption rights with respect to the Additional Shares, any Additional Shares that we propose to issue for cash will first have to be offered to all of our existing shareholders on the same or more favorable terms on a pro-rata basis. As a result of this limitation, we are currently severely limited in the amount of ordinary shares we may sell for cash in any capital raising transaction, and where we propose to issue shares for cash consideration, we may be required to first offer those shares to all of our existing shareholders in a time-consuming pro-rata rights offering. Furthermore, while the statutory pre-emption right applies only to share issuances for cash consideration and it does not apply where we issue shares for non-cash consideration (such as in a share exchange transaction or in any transaction in which property other than cash is received by us in payment for shares), any such transaction would likely be time-consuming and complex to execute. 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 are a clinical-stage pharmaceutical company with a limited operating history. We have not generated any product revenue and have incurred net losses in each year since our inception in 2015. As of December 31, 2023, we had an accumulated deficit of $461.3 million, cash and cash equivalents of $6.1 million and short-term investments of $17.9 million. Our product candidates, oral sulopenem and sulopenem (together, the sulopenem program), are in clinical development, and have not been approved for sale and we may never have our product candidates approved for commercialization. We submitted a New Drug Application (NDA) for oral sulopenem for the treatment of uncomplicated urinary tract infections (uUTIs) in patients with a quinolone non-susceptible pathogen in the fourth quarter of 2020 and the U.S. Food and Drug Administration (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 oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REnewed ASsessment of Sulopenem in uUTI caused by Resistant Enterobacterales (REASSURE), in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024).

We have financed our operations to date primarily with the issuance of 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 Rights Offering) pursuant to which our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), sold units (Units) consisting of (i) Exchangeable Notes; and (ii) Limited Recourse Royalty-Linked Subordinated Notes (RLNs and, together with the Exchangeable Notes, the Securities), 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 an at the market offering agreement (the Sales Agreement) with H.C. Wainwright & Co., LLC (HC Wainwright), as agent, pursuant to which we may offer and sell ordinary shares, nominal value $0.01 per share 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. During the year ended December 31, 2023, we sold 639,825 ordinary shares under the Sales Agreement at an average price of $1.68 per share for net proceeds of $1.0 million. As of December 31, 2023, net proceeds of $16.2 million have been received from the exercise of certain warrants issued as part of the June 30, 2020 Offering, October 2020 Offering and February 2021 Underwritten 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.

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 plan to limit spending to essential costs required in connection with the potential resubmission of the NDA.

We expect to continue to incur significant expenses and increasing operating losses as we conduct clinical trials of oral sulopenem and sulopenem, seek marketing approval for oral sulopenem if clinical trials are successful, engage in pre-commercialization activities 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:

- complete work to support a potential resubmission of our NDA for oral sulopenem;
- initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates and/or may be conducted in response to the CRL;
- establish sales, marketing and distribution capabilities either directly or through a third-party, to commercialize oral sulopenem and/or sulopenem in the United States if we obtain marketing approval from the FDA;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of oral sulopenem and/or sulopenem, 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.

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 expect to continue to incur significant expenses and increasing operating losses as we conduct clinical trials of oral sulopenem and sulopenem, seek marketing approval for oral sulopenem if clinical trials are successful, engage in pre-commercialization activities, and pursue the development of our sulopenem program in additional indications, including through preclinical and clinical development. If we obtain marketing approval for oral sulopenem, sulopenem or any future product candidate and undertake commercialization activities, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Some of these expenses may be incurred in advance of marketing approval, and could be substantial. Additionally, principal and interest on the outstanding Exchangeable Notes become due on January 31, 2025.

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.

Furthermore, under Irish law, our directors may issue new ordinary or preferred shares up to a maximum amount equal to the authorized but unissued share capital 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. We asked our shareholders to renew the authorization of our board of directors to issue shares and the disapplication of statutory pre-emption rights at the 2023 Annual General Meeting of Shareholders (the 2023 Annual Meeting) and to extend that authorization to the increase in authorized share capital that was approved by our shareholders at the 2023 Annual Meeting. Our shareholders renewed the authorization of our board of directors to issue shares; however, we did not receive approval on the disapplication of statutory pre-emption rights. We asked our shareholders to renew the disapplication of statutory pre-emption rights over the authorized but unissued share capital at an extraordinary general meeting of the Company on August 1, 2023; however, although we received over 62% support of the votes cast on renewing the pre-emption rights opt-out authority at that meeting, we did not receive the affirmative vote of at least 75% of the votes cast as required under Irish law for the passing of special resolutions. We asked our shareholders again to approve the disapplication of statutory pre-emption rights over 5,000,000 authorized but unissued ordinary shares at an extraordinary general meeting of the Company on January 30, 2024 (the January EGM) however, again, we did not receive the affirmative vote of at least 75% of the votes cast as required under Irish law for the passing of special resolutions.

If our shareholders do not approve the dis-application of statutory pre-emption rights, our board of director's existing authority to opt out of the statutory pre-emption right up to the amount of our authorized but unissued share capital (excluding the increase in authorized share capital that was approved at the 2023 Annual Meeting) will continue to apply only until January 26, 2026. This would limit us to having the ability to issue for cash only 1.8 million ordinary shares, based on the amount of authorized ordinary shares unissued or unreserved and therefore available for issuance as of February 29, 2024 (excluding the increase in authorized share capital that was approved at the 2023 Annual Meeting), up to January 26, 2026. Furthermore, absent shareholder approval of the dis-application of statutory pre-emption rights, the additional authorized but unissued shares that were approved at the 2023 Annual Meeting that we propose to issue for cash will first have to be offered to all of our existing shareholders on the same or more favorable terms on a pro-rata basis. As a result of this limitation, we are currently severely limited in the amount of ordinary shares we may sell for cash in any capital raising transaction, and where we propose to issue shares for cash consideration, we may be required to first offer those shares to all of our existing shareholders in a time-consuming pro-rata rights offering. Furthermore, while the statutory pre-emption right applies only to share issuances for cash consideration and it does not apply where we issue shares for non-cash consideration (such as in a share exchange transaction or in any transaction in which property other than cash is received by us in payment for shares), any such transaction would likely be time-consuming and complex to execute. While we may seek the approval of our shareholders to disapply the statutory pre-emption rights generally in the future, there is no guarantee that such approval will be forthcoming. In the event we are not able to obtain such shareholder approval of the disapplication of pre-emption rights at a future general meeting of the shareholders, we will continue to be limited in the amount of ordinary shares we may sell for cash in any capital raising transaction without first offering those shares to all of our existing shareholders.

Additional capital will be required in order to repay the Exchangeable Notes when they become due. We may not have enough available cash or be able to obtain financing at that time. Our failure to make repayments when due would constitute a default under the indenture governing the Exchangeable Notes. A default under that indenture could also lead to a default under any agreements governing our future indebtedness.

We expect that additional capital will be required to complete our sulopenem development program and file with regulatory agencies and commercialize oral sulopenem, if regulatory approval is received. If we receive regulatory approval for oral sulopenem, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution. 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 timing and costs of our clinical trials of oral sulopenem and sulopenem, including any clinical trials or non-clinical studies which may be required for regulatory approval of our product candidates;
- any other activities that may be required in connection with the potential resubmission of the NDA for oral sulopenem;
- the timing of regulatory filings including a potential resubmission of the NDA for oral sulopenem;
- the timing of regulatory review and potential approval of any product candidates, including oral sulopenem for the treatment of uUTI;
- 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 commercialization activities for oral sulopenem and/or sulopenem and other product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the receipt of marketing approval and revenue received from any potential commercial sales of oral sulopenem and/or sulopenem;
- the terms and timing of any future collaborations, licensing or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to an exclusive license agreement with Pfizer Inc. (Pfizer) (the Pfizer License) or other future license agreements;
- the amount and timing of any payments we may be required to make in connection with the RLNs and the repayment of the Exchangeable Notes;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;
- the costs of operating as a public company;
- 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. Certain of the derivative values are directly correlated to the value of our ordinary shares. Due to the nature of the required calculations and the large number of ordinary shares involved in such calculations, changes in our share price and/or 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.

Provisions in the EN Indenture and RLN Indenture may deter or prevent us from raising additional capital to fund our operations or entering into a strategic transaction to sell, license, or otherwise dispose of our rights to sulopenem.

Provisions in the agreements we entered into in connection with our financings may deter or prevent us from raising additional capital to fund our operations as and when needed. For example, the indenture governing the Exchangeable Notes (the EN Indenture) contains negative covenants prohibiting our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), as well as us and our wholly owned subsidiaries and their subsidiaries (the Guarantors), who guaranteed Iterum Bermuda's obligations under the Exchangeable Notes, from, among other things, incurring any indebtedness that is not permitted by the EN Indenture and entering into transactions with significant shareholders (as defined in the EN Indenture). In addition, the indenture governing the RLNs (the RLN Indenture) contains negative covenants prohibiting Iterum Bermuda and the Guarantors from, among other things, selling, transferring or assigning certain assets and taking other actions outside the ordinary course of business that would reasonably be expected to reduce the amount of payments under the RLNs.

These provisions could deter or prevent us from raising additional capital or entering into a strategic transaction to sell, license, or otherwise dispose of our rights to sulopenem. 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. Furthermore, our inability to consummate a strategic transaction to sell, license, or otherwise dispose of our rights to sulopenem could impact our ability to maximize stakeholder value.

We are heavily dependent on the success of our sulopenem program, and our ability to develop, obtain marketing approval for and successfully commercialize oral sulopenem and sulopenem. If we are unable to achieve and sustain profitability, the market value of our ordinary shares will likely decline.

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

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

- resolving the matters set out in the CRL received in July 2021 in connection with our NDA for oral sulopenem;
- enrolling and successfully completing any clinical trials that may be required for regulatory approval of our product candidates;
- applying for and obtaining marketing approval for oral sulopenem and/or sulopenem;
- protecting and maintaining our rights to our intellectual property portfolio related to our sulopenem program;
- establishing and maintaining supply and manufacturing relationships with third parties that can support clinical development and can provide adequate commercial quantities of oral sulopenem and/or sulopenem, if approved;
- establishing sales, marketing and distribution capabilities either directly or through a third-party, to commercialize oral sulopenem and/or sulopenem or entering into collaboration arrangements for the commercialization of oral sulopenem and/or sulopenem where we choose not to commercialize directly ourselves; and
- obtaining market acceptance of oral sulopenem and/or sulopenem as viable treatment options.

Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when, or if, we will become profitable. We may never succeed in any or all of these activities and, even if we do, we may never generate revenue that is significant or large enough to achieve profitability. Our expenses could increase if we are required by the FDA, the European Medicines Agency (EMA), or any comparable foreign regulatory authority, to perform different studies or studies in addition to those currently expected, including in response to the CRL received in July 2021, or if there are any delays in completing such studies or with the development of our sulopenem program or any future product candidates. Even if oral sulopenem or sulopenem are approved for commercial sale, we anticipate incurring significant costs associated with the commercial launch of oral sulopenem and/or sulopenem. Where we enter into collaboration arrangements with third-party collaborators for commercialization of product candidates, our product revenues or the profitability of these product revenues to us would likely be lower than if we were to directly market and sell products in those markets.

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

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

The EN Indenture and the RLN Indenture each contain affirmative and negative covenants which impose operating and other restrictions on us, including, among other things, incurring any indebtedness that is not permitted by the EN Indenture or amending the terms of any subordinated indebtedness, entering into strategic transactions or transferring any material assets and undergoing a change of control transaction (subject to certain exceptions, including in the case of a change of control transaction, a transaction in which each holder of an outstanding Exchangeable Note receives cash consideration of at least 300% of the outstanding principal amount of such Exchangeable Notes). For example, pursuant to the EN Indenture, we are required to obtain the consent of a portion of the holders of the Exchangeable Notes prior to entering into collaboration agreements, exclusive selling arrangements or similar partnerships including a definitive agreement for commercialization services in the United States. Failure to comply with these terms could result in an event of default which could lead, among other things, to an acceleration of amounts due under the EN Indenture and the obligation to pay default interest. Moreover, obtaining a consent to a waiver of these terms is subject to a veto right of the holders of 30% of the outstanding Exchangeable Notes, in the case of the EN Indenture, and 30% of the outstanding RLNs, in the case of the RLN Indenture, and 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 rate at which the Exchangeable Notes are exchangeable for our ordinary shares is subject to adjustment, including pursuant to anti-dilution protections. For example, following the sales made under an at the market offering (ATM) pursuant to the Sales Agreement entered into with HC Wainwright, as agent, on October 7, 2022, the exchange rate of the Exchangeable Notes increased and, as of December 31, 2023, the exchange price of the Exchangeable Notes was $11.123 per ordinary share (at an adjusted exchange rate of 89.9035 shares per $1,000 of principal and interest on the Exchangeable Notes). As of December 31, 2023, $11,117 aggregate principal amount of Exchangeable Notes remained outstanding.

Depending on the public offering prices, the number of shares that we sell pursuant to our Sales Agreement with HC Wainwright as agent and any potential increase to the exchange rate of the Exchangeable Notes, we may not have sufficient authorized share capital or share issuance authorities to convert all of the Exchangeable Notes into ordinary shares following any sales of shares pursuant to the Sales Agreement and could be required to settle any exchanges with cash to the extent we do not have available authorized shares. If we elect to settle any exchanges in cash, or we do not have authorized and available ordinary shares needed to satisfy physical exchange of the Exchangeable Notes, our liquidity could be adversely affected and/or we may not have sufficient cash available at that time to satisfy such cash settlement. In addition, in the event we elect to settle exchanges of Exchangeable Notes with ordinary shares, we would be limited in our ability to issue equity for other purposes which could adversely affect our shareholders and our ability to raise additional capital. During the year ended December 31, 2023, we sold 639,825 ordinary shares under the Sales Agreement at an average price of $1.68 per share for net proceeds of $1.0 million.

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.

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

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

Additionally, in the event we are not able to obtain shareholder approval for the disapplication of pre-emption rights over our ordinary shares at a general meeting of the shareholders, we may not be able to efficiently and cost effectively engage in equity-capital raising prior to January 31, 2025, when principal and interest on the outstanding Exchangeable Notes become due.

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. While the EN Indenture restricts our ability to incur additional indebtedness, it allows for certain additional indebtedness and any such restrictions may be waived. If new debt is added to our current debt levels, the related risks that we now face could intensify.

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

Holders of the Exchangeable Notes will have the right to require us to repurchase all or a portion of their Exchangeable Notes upon the occurrence of a fundamental change at specified repurchase prices. In addition, upon exchange of the Exchangeable Notes, unless we elect to deliver solely ordinary shares to settle such exchange (other than paying cash in lieu of delivering any fractional share), we would be required to make specified cash payments in respect of the Exchangeable Notes being exchanged. However, we may not have enough available cash or be able to obtain financing at the time we are required to make repurchases of Exchangeable Notes surrendered therefor or to pay cash with respect to Exchangeable Notes being exchanged. Additionally, in the event we are not able to obtain shareholder approval for the disapplication of pre-emption rights over our ordinary shares at a general meeting of the shareholders, we may not be able to efficiently and cost effectively engage in equity-capital raising prior to January 31, 2025, when principal and interest on the outstanding Exchangeable Notes become due. Our ability to repurchase or to pay cash upon exchange of the Exchangeable Notes may also be limited by law, regulatory authority, and future indebtedness.

Our failure to repurchase Exchangeable Notes at a time when the repurchase is required by the EN Indenture or to pay cash upon exchange of the Exchangeable Notes as required by the EN Indenture would constitute a default under the EN Indenture. A default under the EN Indenture or a fundamental change itself could also lead to a default under agreements governing our future indebtedness. If the payment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and any accrued and unpaid interest and repurchase the Exchangeable Notes or to pay cash upon exchange of the Exchangeable Notes. As of December 31, 2023, $11,117 aggregate principal amount of Exchangeable Notes remained outstanding.

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

Beginning January 21, 2021 and prior to the earlier of (i) the close of business on the scheduled trading day immediately preceding a mandatory exchange notice for the Exchangeable Notes, which would be triggered by the occurrence of any of certain mandatory exchange trigger events specified in the EN Indenture, and (ii) the close of business on the second scheduled trading day immediately preceding the interest record date, holders of Exchangeable Notes are entitled to exchange the Exchangeable Notes at any time at their option. If holders continue to elect to exchange their Exchangeable Notes, unless we elect to satisfy our exchange obligation by delivering solely ordinary shares (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our exchange obligation in cash, which could adversely affect our liquidity. The relevant accounting rules require that we recognize liabilities which appropriately reflect our obligations specified in the EN Indenture. Therefore, even if holders do not elect to exchange their Exchangeable Notes, our liabilities and statement of operations could be significantly impacted.

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 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, nominal value $0.01 per share for aggregate gross sales proceeds of up to $16.0 million (not to exceed 4,478,180), 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.

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.

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. Similarly, while we believe that sulopenem has the potential to treat uUTIs in humans based on the results of prior preclinical studies and clinical trials, oral 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 in our prior Phase 3 uUTI clinical trial. However, in the uUTI clinical 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 CRL from the FDA on July 23, 2021 for 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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024). There can be no assurance that we will be in a position to resolve the matters set forth in the CRL or that the data generated by the REASSURE clinical trial or the additional PK/PD data will be adequate to support resubmission or approval of our NDA.

Further, 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 for uUTI or any other indication or for any other product or to successfully commercialize sulopenem.

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 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 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 trial 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 have engaged a financial advisor to assist management and the board in evaluating strategic alternatives.

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. In the event that we are unable to raise sufficient capital to fund our operations while we evaluate our strategic options, and, if able, consummate a transaction, or identify a viable strategic option at all, our board of directors may determine that a liquidation and dissolution of our business approved by shareholders is the best method to maximize shareholder value.

Risks Related to Clinical Development and Commercialization

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

We currently have no products approved for sale and have invested substantially all of our efforts and financial resources in the development of our sulopenem program. Our near-term prospects are substantially dependent on our ability to develop, apply for and

obtain marketing approval for and successfully commercialize oral sulopenem and/or sulopenem. The success of our sulopenem program will depend on several factors, including the following:

- resolving the issues set out in the CRL received in July 2021 in connection with our NDA for oral sulopenem;
- successful enrollment in, and completion of, clinical trials, including any clinical trials that may be required for regulatory approval of our product candidates;
- clinical trial results with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- timely completion of any additional clinical trials and non-clinical studies conducted to support the filing for regulatory approvals of our sulopenem program, if required by the FDA or any comparable foreign regulatory authority;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment and maintenance of arrangements with third-party manufacturers to obtain commercial supply at a scale sufficient to meet anticipated demand and at a cost appropriate for our commercialization;
- acquisition and maintenance of patent, trade secret and other intellectual property protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain the Pfizer License;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of oral sulopenem and/or sulopenem, if approved, whether alone or in collaboration with others;
- the effectiveness of our own or any future collaborators' marketing, sales and distribution strategy and operations;
- acceptance of oral sulopenem and/or sulopenem, if approved, by patients, physicians and the medical community at large;
- our ability to obtain and sustain coverage and an adequate level of reimbursement by third-party payors;
- the prevalence, frequency and severity of adverse side effects of oral sulopenem and/or sulopenem;
- the availability, perceived advantages, relative cost and relative efficacy of alternative and competing therapies; and
- an acceptable safety profile of oral sulopenem and/or sulopenem following approval.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights, manufacturing and the impact of competition.

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 CRL from the FDA on July 23, 2021 in respect of our NDA. 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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024). There can be no assurance that we will be in a position to resolve the matters set forth in the CRL or that the data generated by the REASSURE clinical trial and/or the additional PK/PD data will be adequate to support resubmission or approval of our NDA. As we work with the FDA to resolve the issues set out in the CRL, we will be delayed in obtaining, and may ultimately be unable to obtain, FDA approval for sulopenem for this or any other indication or for any other product or to successfully commercialize sulopenem.

If we are unable to develop, receive marketing approval for, or successfully commercialize oral sulopenem and/or sulopenem, or if we experience delays as a result of any of these factors or otherwise, our business could be materially harmed.

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

Our company has never obtained regulatory approval for, or commercialized, a drug. We must complete extensive preclinical and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals. To gain approval to market a product candidate, we must provide the FDA and foreign regulatory authorities with non-clinical, clinical and chemistry, manufacturing, and controls (CMC) data that adequately demonstrates the safety and efficacy of the product for the intended indication(s) applied for in the NDA(s) or other respective regulatory filing.

We may never succeed in achieving regulatory approval for any of our product candidates. For example, in the results of our cIAI clinical trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy for the cIAI trial. In the second quarter of 2020, we announced the results of our Phase 3 clinical trials of sulopenem for the treatment of 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 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. 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 prior Phase 3 uUTI trial in which oral sulopenem was statistically superior. 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 CRL from the FDA on July 23, 2021 for our NDA. 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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024). There can be no assurance that we will be in a position to resolve the matters set forth in the CRL and/or that the data generated by the REASSURE clinical trial or the additional PK/PD data will be adequate to support resubmission or approval of our NDA.

We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. Any changes in the outcome of any of these variables with respect to the development of our product candidates in clinical development could mean a significant change in the costs and timing associated with the development of these product candidates.

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

If clinical trials of oral sulopenem, sulopenem or any other product candidate that we may advance to clinical trials fail to demonstrate safety and efficacy to the satisfaction of the FDA or comparable foreign regulatory authorities, or do not otherwise

produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of oral sulopenem, sulopenem or any other product candidate.

We may not commercialize, market, promote, or sell any product candidate in the United States without obtaining marketing approval from the FDA or in other countries without obtaining approvals from comparable foreign regulatory authorities, such as the EMA, and we may never receive such approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. While 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, for which we received a CRL from the FDA on July 23, 2021, we had not previously submitted an NDA to the FDA or similar applications to comparable foreign regulatory authorities for any of our product candidates.

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

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, 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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024). There can be no assurance that we will be in a position to resolve the matters set forth in the CRL or that the data generated by the REASSURE clinical trial and/or the additional PK/PD data will be adequate to support resubmission or approval of our NDA.

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, sulopenem or any of our other product candidates, including:

- although we conducted our prior Phase 3 clinical trials pursuant to SPA agreements, the FDA or other comparable foreign regulatory authorities may ultimately disagree as to the design or implementation of such clinical trials or other clinical trials, or may request additional data to support approval, such as that requested in the CRL from July 2021;
- although we conducted the REASSURE clinical trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) pursuant to an SPA agreement, there is no guarantee that the FDA, or any other regulatory authorities, will approve any application that is supported by a clinical trial conducted in accordance with such agreement;
- we may not reach agreement on acceptable terms with all clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different trial sites;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the FDA, the local National Health Authorities or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have to suspend or terminate clinical trials of a product candidate for various reasons, including non-compliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we enter into agreement for clinical and commercial supplies; or
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

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

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

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 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 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, we may not be able to initiate and/or continue or complete other clinical trials of oral sulopenem, sulopenem or any other product candidate that we develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials as required by the FDA or comparable foreign regulatory authorities, such as the EMA. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

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

The inclusion and exclusion criteria for any clinical trials of oral sulopenem 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 and/or sulopenem, or slow down or halt our product development for oral sulopenem 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 indication.

Although we believe that oral sulopenem and sulopenem have the potential to treat uUTI, cUTI and cIAI in humans based on the results of prior preclinical studies and clinical trials, 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. 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. Similarly, while we believe that sulopenem has the potential to treat uUTI in humans based on the results of prior preclinical studies and clinical trials, and based on our prior Phase 3 uUTI clinical trial, in the population of patients with baseline pathogens resistant to quinolones, in which sulopenem met the related primary endpoint by demonstrating statistical significance in the overall response rate by treatment arm in the ciprofloxacin-resistant population, 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 in our prior Phase 3 uUTI clinical trial. Based on discussions with the FDA at a pre-NDA meeting and previous correspondence with the FDA, we submitted an NDA for oral sulopenem for the treatment of uUTI 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. On July 23, 2021, we received a CRL from the FDA in respect of the NDA. 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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024). There can be no assurance that we will be in a position to resolve the matters set forth in the CRL or that the data generated by the REASSURE clinical trial and/or the additional PK/PD data will be adequate to support resubmission or approval of our NDA.

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

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

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

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 recently completed uUTI trial, REASSURE, patients received either oral sulopenem or Augmentin®. Among 2,214 treated patients, treatment related adverse events were observed in 18.9% and 12.3% of patients on sulopenem 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 sulopenem 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 sulopenem and 0.4% of patients on Augmentin®. Serious adverse events were seen in 0.0% of patients on sulopenem 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 in the CRL received from the FDA in July 2021, in future trials there may be unforeseen serious adverse events or side effects that differ from those seen in our prior Phase 3 program, in Phase 1 normal healthy volunteers with oral sulopenem or the prior post-marketing experience with probenecid. There may also be unexpected adverse events associated with probenecid that have not been seen to date.

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

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

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

- we could be sued and held liable for harm caused to patients;
- our product may become less competitive; and
- our reputation may suffer.

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

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

Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If oral sulopenem, sulopenem or any other product candidate that we develop does not achieve an adequate level of market acceptance, we may not generate significant product revenues and, therefore, we may not become profitable. Market acceptance of any product candidate for which we receive approval depends on a number of factors, including:

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

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

We 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 obtain marketing approval, manufacture a commercial scale product (or arrange for a third party to do so on our behalf), or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products. Assuming we obtain marketing approval for oral sulopenem or sulopenem, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities whether we choose to commercialize product candidates directly ourselves or seek to commercialize them through third-party collaboration arrangements. We may encounter unforeseen expenses, difficulties, complications and delays, and may not be successful in such a transition.

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, oral sulopenem may not be successfully commercialized, if it is approved.

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 strategic transaction with a partner that has established commercial capabilities in the U.S, oral sulopenem may not be successfully commercialized, if it is approved.

We are currently evaluating our commercialization strategy in the United States and other territories. We are focusing our initial commercial efforts on the United States market, which we believe represents the largest market opportunity for our sulopenem program. We currently do not have a sales, marketing or distribution infrastructure and we have no experience in the sales, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either build our marketing, sales, distribution, managerial and other non-technical capabilities, make arrangements to outsource those functions to third parties or enter a strategic transaction with a partner that has established commercial capabilities in the U.S. If oral sulopenem receives regulatory approval, we may build a commercial organization and recruit a targeted sales force with technical expertise, an internal marketing and health resource group, as well as a managed markets group focused on reimbursement activities with third-party payors and a specialty distribution team to ensure pharmacy-level stocking and, where we choose not to commercialize directly ourselves, we will seek to commercialize oral sulopenem collaboration arrangements. 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 July 2021, in order to reduce operating expenses and conserve cash resources, we halted any remaining pre-commercial activities and paused negotiations on the definitive agreement for commercialization services. There is no assurance that we will seek or be able to reach a definitive agreement for commercialization services in the future. Furthermore, while we are currently undergoing a strategic process to sell, license or otherwise dispose of our rights to sulopenem with the goal of maximizing stakeholder value and with the intention of completing such a strategic transaction with a partner that has established commercial capabilities in the U.S., there can be no certainty as to the timing and outcome of our efforts or our ability to consummate such a transaction at all.

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, like COVID-19;
- 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 chose to outsource such services to a third party; and
- our inability to complete a strategic transaction with a partner that has established commercial capabilities in the U.S.

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

There are also a few oral product candidates in clinical development by third parties that are intended to treat uUTIs. Late-stage product candidates include gepotidacin from GlaxoSmithKline and pivmecillinam from Utility Therapeutics Limited. If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

There are several IV-administered products marketed for the treatment of infections resistant to first-line therapy for gram-negative infections, including Avycaz from AbbVie Inc and Pfizer, Vabomere from Melinta Therapeutics, Inc., Zerbaxa from Merck & Co., Zemdri from Cipla, Xerava from Innovia, 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 regulatory exclusivity regardless of whether it is protected by a patent, provided that it is already eligible for another type of regulatory exclusivity. The FDA has designated sulopenem and oral sulopenem as QIDPs for the indications of uUTI, cUTI, cIAI, community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. In December 2016, the Cures Act was passed, providing additional support for the development of new infectious disease products. These incentives may result in more competition in the market for new antibiotics, and may cause pharmaceutical and biotechnology companies with more resources than we have to shift their efforts towards the development of product candidates that could be competitive with oral sulopenem, sulopenem and our other product candidates.

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

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

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

In the United States, sales of our product candidates will depend, in part, on the availability and extent of coverage and reimbursement by third-party payors, such as government health programs, including Medicare and Medicaid, commercial insurance and managed healthcare organizations. There is no uniform coverage and reimbursement policy among third-party payors; however, private third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Obtaining coverage and reimbursement approval for a product candidate from third-party payors is a time-consuming and costly process that may require the provision of supporting scientific, clinical and cost effectiveness data for the use 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 IV, if approved, will be administered in a hospital setting, and oral sulopenem, if approved, will be used in a community setting and possibly be administered in a hospital inpatient setting as well. In the United States, third-party payors generally reimburse hospitals a single bundled payment established on a prospective basis intended to cover all items and services provided to the patient during a single hospitalization. Hospitals bill third-party payors for all or a portion of the fees

associated with the patient's hospitalization and bill patients for any deductibles or co-payments. Because there is typically no separate reimbursement for drugs administered in a hospital inpatient setting, some of our target customers may be unwilling to adopt our product candidates in light of the additional associated cost. If we are forced to lower the price we charge for our product candidates, if approved, our gross margins may decrease, which would adversely affect our ability to invest in and grow our business. Centers for Medicare and Medicaid Services (CMS) recently revised its reimbursement system for certain antibiotics in order to address challenges associated with antimicrobial resistance. Based on the final rule published on August 2, 2019, CMS is finalizing an alternative new technology add-on payment pathway (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 any approved product candidates that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

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

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

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

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

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

- withdrawal of clinical trial volunteers, investigators, patients or trial sites;
- the inability to commercialize our product candidates;
- decreased demand for our product candidates;

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

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

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

If we experience a significant disruption in our information technology systems, or breaches of data security, 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 cyber attack 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.

Risks Related to Our Dependence on Third Parties

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

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

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

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

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

Although we are focusing our initial commercial efforts on the United States market, which we believe represents the largest market opportunity for our sulopenem program, we are also evaluating our commercialization strategy both within and outside the United States. We currently do not have a sales, marketing or distribution infrastructure and we have no experience in the sales, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either build our marketing, sales, distribution, managerial and other non-technical capabilities, or make arrangements to outsource those functions to third parties. For those countries in which we choose not to commercialize directly ourselves, we intend to seek to commercialize oral sulopenem 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 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 July 2021, in order to reduce operating expenses and conserve cash resources, we halted any remaining pre-commercial activities and paused negotiations on a definitive agreement for commercialization services. 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 a product candidate that we license to a third party.

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;

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

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

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 its 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 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, we may not be able to further develop our product candidates or bring them to market 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 product candidates will be significantly impacted and we may be subject to regulatory sanctions.

We may retain third-party service providers to perform a variety of functions related to the sale and distribution of our product candidates, 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 product candidates 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 or commercialize any of our product candidates. If they do not perform satisfactorily, our business may be materially harmed.

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

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

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

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time and resources to our 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 future commercialization of our product candidates and potential product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have the internal infrastructure or capability to manufacture oral sulopenem and sulopenem for use in the conduct of our preclinical research or clinical trials or for commercialization. We rely on third-party contract manufacturers to manufacture supplies of oral sulopenem and sulopenem, and we expect to rely on third-party contract manufacturers to manufacture commercial

quantities of any product candidate that we commercialize following approval for marketing by applicable regulatory authorities, if any. Reliance on third-party manufacturers entails risks, including:

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

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

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

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be approved by the FDA after we submit an NDA(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. In addition, our manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and have a material adverse effect on our business, financial condition and results of operations.

We and our third-party suppliers also continue to refine and improve the manufacturing process, certain aspects of which are complex and unique, and we may encounter difficulties with new or existing processes, particularly as we seek to significantly increase our capacity to commercialize oral sulopenem and/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 in the CRL received from the FDA in July 2021, 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 product candidates.

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

Risks Related to Our Intellectual Property

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

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

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

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

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

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

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

We have sought to protect our proprietary position by in-licensing patents in the United States and abroad related to oral sulopenem. We own two U.S. patents, one Japanese patent, one Korean patent and one Australian patent, with one US 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, and the other US patent directed to the method of use of oral sulopenem in treating multiple diseases,

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

If any patent applications we 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 product candidates, third parties may challenge their ownership, validity, enforceability or scope, which may result in such patents being narrowed, invalidated or held unenforceable, which could allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Any successful opposition to these patents or any other patents owned by us in the future or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Furthermore, even if they are unchallenged, our patents rights may not adequately protect our product candidates and technology, provide exclusivity for our product candidates, prevent others from designing around our claims or provide us with a competitive advantage. Any of these outcomes could impair our ability to prevent competition from third parties. Changes in either the patent laws or interpretation of the patent laws in the United States or other countries may diminish the value of our patent rights or narrow the scope of our patent protection.

We cannot offer any assurances about whether any issued patents will be found invalid and unenforceable or will be challenged by third parties. Any successful challenge or opposition to patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

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

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

We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain

that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, U.S. applications filed before November 29, 2000 and certain U.S. applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

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

Patents have a limited lifespan. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. The patents for our product candidates have varying expiration dates and, if these patents expire, we may be subject to increased competition and we may not be able to recover our development costs. For example, our licensed U.S. patent claim for a composition of matter patent for oral sulopenem is due to expire in 2029, subject to potential extension to 2034 under the Drug Price Competition and Patent Term Restoration Act of 1984 (referred to as the Hatch-Waxman Act) and our newly granted 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. However, that does not guarantee that we will receive any regulatory exclusivity or that any such exclusivity will be for a period sufficient to provide us with any commercial advantage. Moreover, we do not own or license any patent directed to the compound sulopenem.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of the U.S. patents we currently license 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 product candidates;
- issued patents that we may own in the future or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- third parties performing manufacturing or testing for us using our product candidates or technologies could use the intellectual property of others without obtaining a proper license; and
- we may not develop additional proprietary technologies that are patentable.

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

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

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

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the U.S. Patent and Trademark Office (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 oral sulopenem, sulopenem and any future product candidates, if approved, and use our proprietary technologies without alleged or actual infringement, misappropriation or other violation of the patents and other intellectual property rights of third parties. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties.

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

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates, if approved. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee time and resources from our business. Third parties making such claims may have the ability to dedicate substantially greater resources to these legal actions than we or our licensors or collaborators can. In the event of a successful claim of infringement, misappropriation or other violation against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

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

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

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

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

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

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 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 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 oral sulopenem or any other product candidate in the United States must be approved by the FDA, and in Europe by the EMA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA and the EMA each typically conduct a review of proposed product names, including an evaluation of potential for confusion with other product names. We had submitted our proposed proprietary name for oral sulopenem in connection with our NDA for oral sulopenem and we received conditional acceptance from the FDA at that time. However, as provided in the CRL received in July 2021, we are required to resubmit the proposed proprietary name if and when we respond to the application deficiencies and resubmit the NDA for oral sulopenem. There is no guarantee that the FDA will conclude that the proprietary name continues to be acceptable when resubmitted. If the FDA objects to our proposed proprietary product name, 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 oral sulopenem, sulopenem or other future product candidates, and our ability to generate revenue will be materially impaired.

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

Although we have QIDP status and fast track designation for sulopenem and oral sulopenem for the indications of uUTI, cUTI and cIAI (and for the indications of community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease) which may provide for a more rapid 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. We have not obtained regulatory approval for any product candidate and it is possible that we will not be able to obtain regulatory approval for sulopenem or any 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. Although we conducted our prior Phase 3 clinical trials pursuant to SPA agreements, met with the FDA at a pre-NDA meeting and had our NDA application accepted for review by the FDA in January 2021, 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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024). There can be no assurance that we will be in a position to resolve the matters set forth in the CRL or that the data generated by the REASSURE clinical trial and/or the additional PK/PD data will be adequate to support resubmission or approval of our NDA.

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;
- 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.

Further, under the Pediatric Research Equity Act, or PREA, a Biologics License Application, or 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, or 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.

Even if we eventually receive approval of an NDA or foreign marketing application for our product candidates, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, often referred to as Phase 4 clinical trials, and the FDA may require the implementation of a REMS, which may be required to ensure safe use of the drug after approval. The FDA or the applicable regulatory agency also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

Although we conducted the Phase 3 clinical trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) under an SPA agreement with the FDA, an SPA agreement does not guarantee marketing approval of, or any other particular outcome from, regulatory review.

We conducted the Phase 3 clinical trial comparing oral sulopenem and Augmentin® (amoxicillin/clavulanate) under an SPA agreement with the FDA. Under the SPA process, the FDA provides a clinical trial sponsor with an official evaluation and written guidance on the design of a proposed protocol intended to form the basis for an NDA. An SPA agreement indicates concurrence by the FDA with the adequacy and acceptability of specific critical elements of the overall protocol design for a clinical trial intended to support a future marketing application, but it does not indicate FDA concurrence on every protocol detail. An SPA agreement also does not ensure the receipt of marketing approval or that the approval process will be faster than conventional procedures. A determination regarding marketing approval is addressed during the review of a submitted NDA and depends on efficacy and safety results and an evaluation of the overall benefits and risks of treatment after review of the data from the development program in its totality.

Even after the FDA agrees to the design, execution, and analysis proposed in a protocol reviewed under the SPA process, the FDA may revoke or alter its agreement if a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun. An SPA agreement may also be changed through written agreement between the sponsor and the FDA. A revocation or alteration in an existing SPA agreement could delay or prevent approval an NDA. In addition, any significant change to the protocol for a clinical trial subject to an SPA agreement would require prior FDA approval, which could delay implementation of such a change and the conduct of the related clinical trial. The FDA retains significant discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

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 our product candidates outside of the United States.

In order to market and sell oral sulopenem, sulopenem or our other future product candidates in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. For example, although we have obtained agreement on an SPA with the FDA for the additional Phase 3 clinical trial for oral sulopenem, the EMA or other regulatory authorities may not agree with the overall protocol design for this additional clinical trial. 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.

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

Additionally, we could face heightened risks with respect to obtaining marketing authorization in the UK as a result of the withdrawal of the UK from the EU, commonly referred to as Brexit. The UK is no longer part of the European Single Market and EU Customs Union. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, became responsible for supervising medicines and medical devices in Great Britain,, or GB, comprising England, Scotland and Wales under domestic law, whereas under the terms of the Northern Ireland Protocol, Northern Ireland is currently subject to EU rules. The UK and EU have however agreed to the Windsor Framework which fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK Once implemented, the changes introduced by the Windsor Framework will see the MHRA be responsible for approving all medicinal products destined for the UK market (i.e., GB and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. Any delay in obtaining, or an inability to obtain, any marketing authorizations, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the UK 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.

If we receive regulatory approval for any product candidate, we will be subject to ongoing obligations and continuing regulatory review, which may result in significant additional expense. Our product candidates, including oral sulopenem and sulopenem, if

approved, could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if approved.

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

In addition, even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed, may be subject to significant conditions of approval or may impose requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

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 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 products and assuming we, or our collaborators, receive marketing approval for one or more of our 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 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. 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, or the 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, or 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, or the 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.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new executive order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this executive order, federal agencies are directed

to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

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

In the EU, on December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment, or 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, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or 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. Nine states (Colorado, Florida, Maine, New Hampshire, New Mexico, North Dakota, Texas, Vermont and Wisconsin) have passed laws allowing for the importation of drugs from Canada. Certain of these states have submitted Section 804 Importation Program proposals and are awaiting FDA approval. On January 5, 2023, the FDA approved Florida's plan for Canadian drug importation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which has been delayed until January 1, 2032 by the Inflation Reduction Act, or IRA.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. To address these costs, the executive order directs HHS to create a plan within 45 days to combat "excessive pricing of prescription drugs and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such drugs, and to address the recurrent problem of price gouging." Thereafter, on September 9, 2021, HHS released its plan to reduce drug prices. The key features of that plan are to: (a) make drug prices more affordable and equitable for all consumers and throughout the health care system by supporting drug price negotiations with manufacturers; (b) improve and promote competition throughout the

prescription drug industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

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.

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. 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 European Economic Area (EEA), in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data (including health and other sensitive data), including the following: to provide information to individuals regarding data processing activities; to implement safeguards to protect the security and confidentiality of personal data; to make a mandatory breach notification in certain circumstances; and to take certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the 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.

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 or in the event we are successful in obtaining regulatory approval 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 Securities in accordance with the terms and conditions of the EN Indenture and 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 Securities. 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, or "QEF election," under the U.S. federal income tax laws with respect to that holder's interest in a PFIC. Such an election may mitigate some of the adverse U.S. federal income tax consequences that could otherwise apply to a U.S. Holder under the excess distribution regime. However, we do not expect to provide U.S. Holders with the information necessary to make a valid QEF election, and 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 $2.30 on November 24, 2023, and a low price of $0.65 on October 25, 2023, in the twelve-month period ending on March 26, 2024. During this time, the price per ordinary share has ranged from an intra-day low of $0.622 per share to an intra-day high of $2.50 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 oral sulopenem, sulopenem or any future product candidates;
- manufacturing and supply issues related to our development programs and commercialization of oral sulopenem, 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 oral sulopenem, 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. For example, we asked our shareholders to approve the disapplication of statutory pre-emption rights over the increased authorized share capital that was approved by our shareholders at our annual general meeting of shareholders in May 2023 (the 2023 Annual Meeting). However,

we did not receive the affirmative vote of at least 75% of the votes cast as required under Irish law for the passing of such resolutions at the 2023 Annual Meeting or at subsequent extraordinary general meetings of shareholders held in August 2023 and January 2024. As a result, our ability to raise additional capital to finance our business through the issue of new shares for cash is severely limited. Additionally, where we find it necessary to delay or adjourn meetings or to seek approval again, 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. The delisting of our ordinary shares from The Nasdaq Stock Market could also negatively impact our financial condition as it would constitute a fundamental change under the EN Indenture, which could trigger an obligation for us to repurchase the Exchangeable Notes at a repurchase price of 300% of the principal amount of the outstanding Exchangeable Notes.

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

As part of a private placement which closed in January 2020 (the Private Placement) and subsequent rights offering (the 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 (Payment Rate), determined based on which of the specified sulopenem products have received FDA approval. The Payment Rate will be based on the maximum aggregate principal amount of RLNs and will equal (i) up to 15% if we or one of our affiliates has received FDA approval for the use of specified sulopenem products for the treatment of uUTIs and (ii) up to 20% if we or one of our affiliates has received FDA approval for the use of specified sulopenem products for the treatment of cUTIs but has not received FDA approval for treatment of uUTIs.

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. In the event that a change of control occurs before we receive FDA approval with respect to one or more specified sulopenem products, the redemption price per RLN will be reduced to 50% of the Maximum Return for each RLN, less payments made through and including the redemption date, plus certain accrued but unpaid default interest (if any).

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

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

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

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.

In addition, the Exchangeable Notes are exchangeable for ordinary shares, cash or a combination of ordinary shares and cash, at our election, upon the terms and conditions specified therein. If we elect for physical settlement, the issuance of ordinary shares for the Exchangeable Notes may dilute the ownership percentage or voting power of our shareholders. As of December 31, 2023, $11,117 aggregate principal amount of Exchangeable Notes remained outstanding. 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 and the February 2021 Registered Direct 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, the Exchangeable Notes are exchangeable for our ordinary shares upon the terms and conditions specified therein and a substantial portion have been exchanged for our ordinary shares. Pursuant to the investor rights agreement we entered into in connection with the Private Placement, we have filed a registration statement covering the resale of the ordinary shares issuable in connection with the exchange of the Exchangeable Notes issued as part of the Private Placement, among other securities, and the

resale of the ordinary shares issuable in connection with the exchange of the Exchangeable Notes issued in connection with the Rights Offering are also covered by a registration statement.

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, nominal value $0.01 per share for aggregate gross sales proceeds of up to $16.0 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. 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 an "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 EN Indenture and RLN Indenture may deter or prevent a business combination that may be favorable to the holders of our ordinary shares.

If a fundamental change occurs prior to the interest record date of the Exchangeable Notes, holders of the Exchangeable Notes will have the right, at their option, to require us to repurchase for cash all or a portion of their Exchangeable Notes for the greater of (i) 300% of the principal amount thereof, and (ii) the consideration that would be received by the holder of such note in connection with a transaction if the holder had exchanged the note for Ordinary Shares immediately prior to the consummation of such transaction. The negative covenants in the EN Indenture also prohibit us from undergoing a change of control transaction, other than a transaction in

which each Exchangeable Note holder receives cash consideration of at least 300% of the outstanding principal amount of its notes. Furthermore, the EN Indenture prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the Exchangeable Notes, the EN Indenture and the guarantees. In addition, the RLN Indenture prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the RLNs, the RLN Indenture and the guarantees and the RLN Indenture prohibits us from selling, transferring or assigning certain assets and prohibits Iterum Bermuda, the Guarantors or any of our significant subsidiaries from undergoing a change of control, other than in connection with a change of control of us. These and other provisions in the EN Indenture and the RLN Indenture could deter or prevent a third party from acquiring us even when the acquisition may be favorable to the holders of our ordinary shares.

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

Following the authorization for trading of our ordinary shares on the Nasdaq Global Market 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. The EN Indenture provides that if a holder of Exchangeable Notes notifies us that they would be subject to this mandatory offer requirement, we will only issue to such holder such number of ordinary shares that can be issued without triggering a mandatory cash offer on an exchange with the remaining ordinary shares to be delivered as promptly as practicable after the holder notifies us that they would no longer be subject to a mandatory cash offer request.

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 and the other holders of the Exchangeable Notes to acquire more of our securities, including under the terms of the Exchangeable Notes and 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 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. We asked our shareholders to renew the authorization of our board of directors to issue shares and the disapplication of statutory pre-emption rights at our 2023 Annual Meeting and to extend that authorization to the increase in authorized share capital that was approved by our shareholders at the 2023 Annual Meeting. Our shareholders renewed the authorization of our board of directors to issue shares; however, we did not receive approval on the disapplication of statutory pre-emption rights. We asked our shareholders to

renew the disapplication of statutory pre-emption rights over the authorized but unissued share capital at an extraordinary general meeting of the Company on August 1, 2023; however, although we received over 62% support of the votes cast on renewing the pre-emption rights opt-out authority at that meeting, we did not receive the affirmative vote of at least 75% of the votes cast as required under Irish law for the passing of special resolutions. We asked our shareholders again to approve the disapplication of statutory pre-emption rights over 5,000,000 authorized but unissued ordinary shares at an extraordinary general meeting of the Company on January 30, 2024; however, again, we did not receive the affirmative vote of at least 75% of the votes cast as required under Irish law for the passing of special resolutions.

If our shareholders do not approve the dis-application of statutory pre-emption rights, our board of director's existing authority to opt out of the statutory pre-emption right up to the amount of our authorized but unissued share capital (excluding the increase in authorized share capital that was approved at the 2023 Annual Meeting) will continue to apply only until January 26, 2026. This would limit us to having the ability to issue for cash only 1.8 million ordinary shares, based on the amount of authorized ordinary shares unissued or unreserved and therefore available for issuance as of February 29, 2024 (excluding the increase in authorized share capital that was approved at the 2023 Annual Meeting), up to January 26, 2026. Furthermore, absent shareholder approval of the dis-application of statutory pre-emption rights, the additional authorized but unissued shares that were approved at the 2023 Annual Meeting that we propose to issue for cash will first have to be offered to all of our existing shareholders on the same or more favorable terms on a pro-rata basis. As a result of this limitation, we are currently severely limited in the amount of ordinary shares we may sell for cash in any capital raising transaction, and where we propose to issue shares for cash consideration, we may be required to first offer those shares to all of our existing shareholders in a time-consuming pro-rata rights offering. Furthermore, while the statutory pre-emption right applies only to share issuances for cash consideration and it does not apply where we issue shares for non-cash consideration (such as in a share exchange transaction or in any transaction in which property other than cash is received by us in payment for shares), any such transaction would likely be time-consuming and complex to execute. While we currently intend to again seek the approval of our shareholders to disapply the statutory pre-emption rights generally, there is no guarantee that such approval will be forthcoming. In the event we are not able to obtain such shareholder approval of the disapplication of pre-emption rights at a future general meeting of the shareholders, we will continue to be limited in the amount of ordinary shares we may sell for cash in any capital raising transaction without first offering those shares to all of our existing shareholders.

Since our inception, we have primarily funded our research and development activities, the commercialization of our products and our operations from the sale of equity securities. We will need to obtain substantial additional funding to achieve our business objectives. If we are unable to raise additional funds when needed, including through the sale of our ordinary shares for cash, we may be unable to pursue our business plans and strategy, and we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Therefore, we believe obtaining shareholder approval of the pre-emption rights dis-application proposal at a future general meeting of the shareholders is critical to our ability to continue to fund our operations and achieve our business objectives.

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 Securities and Exchange Commission. 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.

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 is responsible for the day-to-day management of risks we face and is involved in implementing the IR Plan, with assistance from our third-party IT service 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.

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.

Our headquarters are located in Dublin, Ireland, where we hold a license for office space through July 2024.

In June 2018 we entered into a lease for a commercial unit in Dublin that extended through June 2038 (the Term), with the option to terminate the lease in June 2028 with no penalty provided one year's notice is given. A deed of assignment was signed in August 2023 in relation to this lease assigning the remainder of the Term to a third party.

We also 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 November 2024.

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 February 29, 2024, we had 5 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, 2023 through December 31, 2023, 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. Unless otherwise stated herein, all ordinary shares, exchange rates for the Exchangeable Notes, equity awards, warrants and per share amounts have been adjusted to reflect the 1-for-15 reverse share split which became effective on August 17, 2022, for all prior periods presented.

Overview

We are a clinical-stage pharmaceutical company dedicated to developing and commercializing sulopenem to be potentially the first oral branded penem available in the United States and the first and only oral and intravenous (IV) branded penem available globally. Penems, including thiopenems and carbapenems, belong to a class of antibiotics more broadly defined as ß-lactam antibiotics, the original example of which was penicillin, but which now also includes cephalosporins. Sulopenem is a potent, thiopenem antibiotic delivered intravenously which is active against bacteria that belong to the group of organisms known as gram-negatives and cause urinary tract and intra-abdominal infections. We have also developed sulopenem in an oral tablet formulation, sulopenem etzadroxil-probenecid, which we refer to herein as oral sulopenem. We believe that sulopenem and oral sulopenem have the potential to be important new treatment alternatives to address growing concerns related to antibacterial resistance without the known toxicities of some of the most widely used antibiotics, specifically fluoroquinolones.

During the third quarter of 2018, we initiated three clinical trials in our Phase 3 development program which included: a Phase 3 uncomplicated urinary tract infection (uUTI) clinical trial, known as Sulopenem for Resistant Enterobacteriaceae (SURE) 1, comparing oral sulopenem to oral ciprofloxacin in women with uUTI, a Phase 3 complicated urinary tract infection (cUTI) clinical trial known as SURE 2, comparing IV sulopenem followed by oral sulopenem to IV ertapenem followed by oral ciprofloxacin in adults with cUTI and a Phase 3 complicated intra-abdominal infection (cIAI) clinical trial known as SURE 3, comparing IV sulopenem followed by oral sulopenem to IV ertapenem followed by a combination of oral ciprofloxacin and oral metronidazole in adults with cIAI. We designed one Phase 3 clinical trial in each indication based on our end of Phase 2 meeting with the U.S. Food and Drug Administration (FDA) and feedback from the European Medicines Agency (EMA). We conducted the Phase 3 clinical trials under Special Protocol Assessment (SPA) agreements from the FDA. 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. 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 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-New Drug Application (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 SPA process on the design, endpoints and statistical analysis of a Phase 3 clinical trial for oral sulopenem for the treatment of uUTIs and we commenced enrollment in that clinical trial, known as REnewed ASsessment of Sulopenem in uUTI caused by Resistant Enterobacterales (REASSURE), in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our

NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024).

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 successful development and eventual commercialization of oral sulopenem and sulopenem. As of December 31, 2023, we had an accumulated deficit of $461.3 million. We expect to continue to incur significant expenses for the foreseeable future as we complete work to support a potential resubmission of our NDA for oral sulopenem. In addition, if we obtain marketing approval for oral sulopenem, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Additionally, principal and interest on the outstanding Exchangeable Notes become due on January 31, 2025. We may also incur expenses in connection with the further clinical development of IV sulopenem and clinical development of sulopenem in additional indications, the establishment of additional sources for the manufacture of 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 additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

As a result, we will require additional capital to fund our operations, to continue to develop our sulopenem program and to execute our strategy. Until such time as we can obtain marketing approval for oral sulopenem, sulopenem or any future product candidate and generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements, marketing and distribution arrangements or government funding. However we may be unable to obtain such financing when needed or on acceptable terms. Additionally, in the event we are not able to obtain shareholder approval for the disapplication of pre-emption rights over our ordinary shares at a general meeting of the shareholders, our ability to raise additional capital through the issue of new shares for cash will be severely limited.

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 and commercialization of our sulopenem program. As of December 31, 2023, we had cash, cash equivalents and short-term investments of $23.9 million. Based on our available cash resources, including amounts raised subsequent to the year end under the "at-the-market" agreement, as disclosed in Note 17 − Subsequent Events, we do not believe that our existing cash, cash equivalents and short-term investments 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 including through repayment of the 6.500% Exchangeable Senior Subordinated Notes due in January 2025 (Exchangeable Notes). 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 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, the Company's ability to raise additional capital through the issue of new shares for cash is limited to issuing only 1.8 million ordinary shares (or rights to acquire such shares) for cash, based on the amount of authorized ordinary shares unissued or unreserved and free from any statutory rights of pre-emption, and therefore available for issuance as of February 29, 2024. While shareholders approved an increase of an additional 60,000,000 ordinary shares at our annual general meeting in May 2023 (the Additional Shares), we did not receive approval for the disapplication of statutory pre-emption rights over such shares. Absent shareholder approval of the dis-application of statutory pre-emption rights with respect to the Additional Shares, any Additional Shares that we propose to issue for cash will first have to be offered to all of our existing shareholders on the same or more favorable terms on a pro-rata basis. As a result of this limitation, we are currently severely limited in the amount of ordinary shares we may sell for cash in any capital raising transaction, and where we propose to issue shares for cash consideration, we may be required to first offer those shares to all of our existing shareholders in a time-consuming pro-rata rights offering. Furthermore, while the statutory pre-emption right applies only to share issuances for cash consideration and it does not apply where we issue shares for non-cash consideration (such as in a share exchange transaction or in any transaction in which property other than cash is received by us in payment for shares), any such transaction would likely be time-consuming and complex to execute.

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 stakeholders and have 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—Liquidity and Going Concern" 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

Operating Expenses

Research and Development Expenses

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

- expenses incurred under agreements with contract research organizations (CROs), contract manufacturing organizations (CMOs), as well as investigative sites and consultants that conduct our clinical trials, preclinical studies and other scientific development services;
- manufacturing scale-up expenses and the cost of acquiring and manufacturing preclinical and clinical trial materials and commercial materials, including manufacturing validation batches 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.

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

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

We may never succeed in achieving regulatory approval for any of our product candidates. For example, in the results of our cIAI clinical trial, sulopenem did not meet the primary endpoint of statistical non-inferiority compared to the control therapy for the cIAI trial. In the second quarter of 2020, we announced the results of our Phase 3 clinical trials of sulopenem for the treatment of 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 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. 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. 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 CRL from the FDA on July 23, 2021, for our NDA. 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 we commenced enrollment in that clinical trial, known as REASSURE, in October 2022. The study is 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 sulopenem 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). We have also completed the additional non-clinical PK/PD investigations, as recommended by the FDA, which we believe support the dosing regimen selected for oral sulopenem. We expect to resubmit our NDA to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the CRL we received from the FDA in July 2021, we expect that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024). There can be no assurance that we will be in a position to resolve the matters set forth in the CRL or that the data generated by the REASSURE clinical trial and/or the additional PK/PD data will be adequate to support resubmission or approval of our NDA.

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.

Following receipt of the CRL in the third quarter of 2021 we halted all remaining pre-commercial activities for oral sulopenem. Payroll and expenses may increase in preparation for commercial operations if regulatory approval of oral sulopenem appears likely.

Interest Expense, Net

Interest expense, net consists of interest accrued and amortization of debt costs with respect to the Exchangeable Notes and Limited Recourse Royalty-Linked Subordinated Notes (RLNs) issued in 2020 (through January 2021), 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, interest earned on our investments in marketable securities and interest incurred and amortization of debt costs on our loan from Silicon Valley Bank (SVB) (fully repaid in March 2022) and interest incurred on our note received under the Payment Protection Program (the PPP loan) (fully repaid in March 2022). Interest on the Exchangeable Notes is 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 becomes due and payable.

Adjustments to Fair Value of Derivatives

Derivative liabilities, which consist of the RLNs and the embedded features in the Exchangeable Notes, 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 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 (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.

Accrued Research and Development Expenses

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

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

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which

services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Share-Based Compensation

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

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

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

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

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

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

We have elected to account for forfeitures as they occur.

Derivative Liability

We account for derivative instruments in accordance with Accounting Standard Codification (ASC) 815, *Derivatives and Hedging – Contracts in Entity's Own Equity,* 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 each reporting period with the resulting change in fair value reflected in the consolidated statements of operations as adjustments to fair value of derivatives.

Our derivative financial instruments consist of embedded features in the Exchangeable Notes. The embedded derivatives include provisions that provide the noteholder with certain exchange rights and protections on a fundamental change such as a change of control. The effects of interactions between embedded derivatives are calculated and accounted for in arriving at the overall fair value of the financial instruments. In determining the appropriate fair values, we use the binomial option pricing model, and in the case of the change of control component, in combination with a discounted cash flow (DCF) analysis.

The binomial option-pricing model uses certain key inputs and assumptions including share price and share price volatility, the exchange rate, risk-free interest rate and dividend yield. Many of the assumptions require significant judgment and any changes could have a material impact in the determination of the derivative liability balances.

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, probability of regulatory approval of sulopenem, 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, 2023 and 2022

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

	Year Ended December 31,		
	2023	2022	Change
	(In thousands)		
Operating 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 (case cannot be brought back to court) in January 2023.

The following table summarizes our total other 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 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.

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our operating loss and loss before tax for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		
	2022	2021	Change
	(In thousands)		
Operating expenses:			
Research and development	$ (17,617)	$ (10,712)	$ (6,905)
General and administrative	(12,766)	(13,825)	1,059
Total operating expenses	$ (30,383)	$ (24,537)	$ (5,846)
Operating loss	(30,383)	(24,537)	(5,846)
Total other expense	(13,750)	(66,322)	52,572
Loss before income taxes	$ (44,133)	$ (90,859)	$ 46,726

Research and Development Expenses

	Year Ended December 31,		
	2022	2021	Change
	(In thousands)		
CRO and other preclinical and clinical trial expenses	$ 9,374	$ 2,153	$ 7,221
Personnel related (including share-based compensation)	4,446	2,630	1,816
Chemistry, manufacturing and control (CMC) related expenses	2,642	2,981	(339)
Consulting fees	1,155	2,948	(1,793)
Total research and development expenses	$ 17,617	$ 10,712	$ 6,905

The increase in CRO and other preclinical and clinical trial expenses of $7.2 million was primarily due to an increase in costs incurred to support our REASSURE clinical trial, which began enrollment in October 2022. Personnel related expenses increased by $1.8 million as a result of an increase in headcount. Personnel related expenses for the years ended December 31, 2022 and 2021

included share-based compensation expense of $1.4 million and $1.3 million, respectively. CMC related expenses decreased by $0.3 million primarily due to process qualification work completed in 2021. The decrease in consulting fees of $1.8 million was primarily due to a decrease in consultants used for research and development activities in 2022. Consulting fees for the year ending December 31, 2021 primarily related to consultants used during the FDA review of our NDA for oral sulopenem.

General and Administrative Expenses

	Year Ended December 31,		
	2022	2021	Change
		(In thousands)	
Personnel related (including share-based compensation)	$ 6,153	$ 4,870	$ 1,283
Facility related and other	3,527	3,416	111
Professional and consultant fees	3,086	5,539	(2,453)
Total general and administrative expenses	$ 12,766	$ 13,825	$ (1,059)

Personnel related expenses increased by $1.3 million primarily as a result of an increase in compensation and headcount. Personnel related expenses for the years ended December 31, 2022 and 2021 included share-based compensation expense of $2.8 million and $2.7 million, respectively. Facility related and other costs increased by $0.1 million primarily as a result of an increase in directors' fees and directors' share-based compensation, partially offset by a reduction in rent expense. Facility related and other costs for the years ended December 31, 2022 and 2021 included directors' share-based compensation expense of $0.6 million and $0.3 million, respectively. Professional and consulting fees decreased by $2.5 million primarily as a result of pre-commercialization activities carried out in 2021 prior to receipt of the CRL and a decrease in consultants used to support our general and administrative functions, partially offset by an increase in legal fees associated with the lawsuit filed in August 2021 which was dismissed with prejudice (case cannot be brought back to court) in January 2023.

The following table summarizes our total other expense for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		
	2022	2021	Change
		(In thousands)	
Interest expense, net	$ (2,361)	$ (5,553)	$ 3,192
Adjustments to fair value of derivatives	5,458	(60,964)	66,422
Cancellation of share options	(17,350)	—	(17,350)
Other income, net	503	195	308
Total other expense	$ (13,750)	$ (66,322)	$ 52,572

Interest Expense, Net

Interest expense, net decreased by $3.2 million for the year ended December 31, 2022 primarily as a result of a decrease in the amortization of the debt discounts and deferred financing costs relating to the RLNs which were listed, and therefore fully amortized, in January 2021, a decrease in interest accruing on our Exchangeable Notes and a decrease in the amortization of the debt discounts and deferred financing costs relating to them due to the reduction in the Exchangeable Notes outstanding balance and a reduction in interest expense associated with our credit facility with SVB, which was repaid in full in March 2022, and a decrease in unrealized losses on our short-term investments.

Adjustments to Fair Value of Derivatives

Adjustments to the fair value of the Derivative liability were $5.5 million and $61.0 million for the years ended December 31, 2022 and 2021, respectively. 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. This non-cash adjustment in 2021 related to an increase in the value of derivative components associated with the Exchangeable Notes that were exchanged in the first half of 2021 and an increase in the fair value of our RLNs, partially offset by a decrease in the value of the derivative components associated with the remaining Exchangeable Notes.

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 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.

Liquidity and Capital Resources

Under Irish law, our board of directors may issue new ordinary or preferred shares up to a maximum amount equal to the authorized but unissued share capital once authorized to do so by our articles of association or by an ordinary resolution of our shareholders. Additionally, subject to specified exceptions, Irish law grants statutory 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 special resolution. Such disapplication can either be generally applicable or be in respect of a particular allotment of shares. Our board of directors was initially authorized under our articles of association to issue new shares, and to disapply statutory pre-emption rights. The authorization of our board of directors to issue shares and the disapplication of statutory pre-emption rights must both be renewed by the shareholders at least every five years. We asked our shareholders to renew the authorization of our board of directors to issue shares and the disapplication of statutory pre-emption rights at our 2023 Annual General Meeting of Shareholders (2023 Annual Meeting), and to extend that authorization to the increase in authorized share capital that was approved by our shareholders at the 2023 Annual Meeting. Our shareholders renewed the authorization of our board of directors to issue shares; however, we did not receive approval on the disapplication of statutory pre-emption rights. We asked our shareholders to renew the disapplication of statutory pre-emption rights over the authorized but unissued share capital at an extraordinary general meeting of the Company on August 1, 2023; however, although we received over 62% support of the votes cast on renewing the pre-emption rights opt-out authority at that meeting, we did not receive the affirmative vote of at least 75% of the votes cast as required under Irish law for the passing of special resolutions. We asked our shareholders again to approve the disapplication of statutory pre-emption rights over 5,000,000 authorized but unissued ordinary shares at an extraordinary general meeting of the Company on January 30, 2024; however, again, we did not receive the affirmative vote of at least 75% of the votes cast as required under Irish law for the passing of special resolutions.

If our shareholders do not approve the dis-application of statutory pre-emption rights, our board of director's existing authority to opt out of the statutory pre-emption right up to the amount of our authorized but unissued share capital (excluding the increase in authorized share capital that was approved at the 2023 Annual Meeting) will continue to apply only until January 26, 2026. This would limit us to having the ability to issue for cash only 1.8 million ordinary shares, based on the amount of authorized ordinary shares unissued or unreserved and therefore available for issuance as of February 29, 2024 (excluding the increase in authorized share capital that was approved at the 2023 Annual Meeting), up to January 26, 2026. Furthermore, absent shareholder approval of the dis-application of statutory pre-emption rights, the additional authorized but unissued shares that were approved at the 2023 Annual Meeting that we propose to issue for cash will first have to be offered to all of our existing shareholders on the same or more favorable terms on a pro-rata basis. As a result of this limitation, we are currently severely limited in the amount of ordinary shares we may sell for cash in any capital raising transaction, and where we propose to issue shares for cash consideration, we may be required to first offer those shares to all of our existing shareholders in a time-consuming pro-rata rights offering. Furthermore, while the statutory pre-emption right applies only to share issuances for cash consideration and it does not apply where we issue shares for non-cash consideration (such as in a share exchange transaction or in any transaction in which property other than cash is received by us in payment for shares), any such transaction would likely be time-consuming and complex to execute. While we may seek the approval of our shareholders to disapply the statutory pre-emption rights generally in the future, there is no guarantee that such approval will be forthcoming. In the event we are not able to obtain such shareholder approval of the disapplication of pre-emption rights at a future general meeting of the shareholders, we will continue to be limited in the amount of ordinary shares we may sell for cash in any capital raising transaction without first offering those shares to all of our existing shareholders.

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 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, 2023, we had received cash proceeds of $198.2 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 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 and net proceeds of $32.2 million from the registered direct offering in February 2021 (February 2021 Registered Direct 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 a sales agreement (the Sales Agreement), with H.C. Wainwright & Co., LLC (HC Wainwright), as agent, pursuant to which we may offer and sell ordinary shares, nominal value $0.01 per share, 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. During the year ended December 31, 2023, we sold 639,825 ordinary shares under the Sales Agreement at an average price of $1.68 per share for net proceeds of $1.0 million, after deducting commissions to HC Wainwright of $0.03 million.

As of December 31, 2023, we had cash, cash equivalents and short-term investments of $23.9 million.

Secured credit facility

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

Required monthly amortization payments for the initial $15.0 million draw commenced on November 1, 2019 and total principal repayments of $1,552 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 repaid on March 1, 2022 (the maturity date), effectively terminating the Loan and Security Agreement. The final payment fee of $0.6 million 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 $15.0 million draw, we issued SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B convertible preferred shares (which converted into warrants to purchase 1,326 ordinary shares upon our IPO) at an exercise price of $282.75 per share. These warrants will expire on April 27, 2028.

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 to, among other things, modify the definition of subordinated debt to include the RLNs and Exchangeable Notes.

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 are exchangeable for our ordinary shares, cash or a combination of ordinary shares and cash, at an exchange rate of 89.9035 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an exchange price of approximately $11.123 per ordinary share) as of December 31, 2023, 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 is subject to further adjustment pursuant to the terms of the Exchangeable Notes Indenture. The Exchangeable Notes will mature on January 31, 2025. Beginning on January 21, 2021 to December 31, 2023, 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, 2023 was $11.1 million. 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 up to either 15% or 20% of net revenues from U.S. sales of such products, depending on the indication approved by the FDA. The aggregate amount of payments on each RLN is capped at $160.00 (or 4,000 times the principal amount of such RLN). Iterum Bermuda received net proceeds from the sale of the 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 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.

Payment Protection Program

In April 2020, we began deferring payment on our share of U.S. payroll taxes owed, as allowed by the CARES Act through December 31, 2020. We paid half of our share of the 2020 U.S. payroll taxes owed in December 2021, with the remaining half paid in December 2022.

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 (the Borrower), entered into the PPP loan with SVB under the Paycheck Protection Program, pursuant to the Borrower receiving a loan of $0.7 million with a fixed 1% annual interest rate and a maturity of two years. Under the terms of the agreement, there were no payments due until the earlier of the SBA remitting the forgiveness amount to the Borrower or 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 $0.3 million of the loan in November 2020, and the remaining loan of $0.4 million began amortization in December 2020 with equal monthly repayments of $26 through March 2022. All outstanding amounts, including the final interest payment, were repaid on March 17, 2022, effectively terminating the PPP loan.

Cash Flows

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

	Year Ended December 31,		
	2023	2022	2021
	(In thousands)		
Net cash used in operating activities	$ (39,330)	$ (18,473)	$ (15,842)
Net cash provided by / (used in) investing activities	23,336	13,957	(54,595)
Net cash provided by / (used in) financing activities	1,034	(1,818)	83,127
Effect of exchange rates on cash and cash equivalents	(61)	(50)	4
Net (decrease) / increase in cash, cash equivalents and restricted cash	$ (15,021)	$ (6,384)	$ 12,694

Operating Activities

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.

During the year ended December 31, 2021, operating activities used $15.8 million of cash, resulting from our net loss of $91.6 million and net cash used by changes in our operating assets and liabilities of $0.4 million, partially offset by non-cash charges of $76.2 million. Net cash used by changes in our operating assets and liabilities for the year ended December 31, 2021 consisted primarily of decreases in other liabilities and accrued expenses, offset by a decrease in prepaid expenses and other current assets, primarily due to the refund of the FDA filing fees of $2.9 million received in January 2021.

Investing Activities

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. During the year ended December 31, 2021, net cash used in investing activities was primarily related to purchases of short-term investments of $67.0 million, partially offset by sales of short-term investments of $12.5 million.

Financing Activities

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. During the year ended December 31, 2021, net cash provided by financing activities was $83.1 million and consisted of net cash proceeds of $42.1 million from the February Underwritten Offering, net cash proceeds of $32.2 million from the February Registered Direct Offering and $15.3 million from the exercise of warrants, partially offset by principal repayments of $6.5 million made to SVB under the Loan and Security Agreement and the PPP loan.

Funding Requirements

We expect to continue to incur significant expenses and increasing operating losses as we seek potential marketing approval for oral sulopenem, resume any pre-commercialization activities and pursue the development of our sulopenem program in additional indications through preclinical and clinical development.

As of December 31, 2023, we had cash, cash equivalents and short-term investments of $23.9 million, and subsequent to the year-end through the date of this filing we received net proceeds of $7.1 million from the sale of our ordinary shares under the "at-the-market" agreement with HC Wainwright. For more information see Note 17 — Subsequent Events. 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, cash equivalents and short-term investments, including amounts raised subsequent to the year-end, will enable us to fund our operating expenses for the next 12 months from the date of this Annual Report on Form 10-K including repayment of the Exchangeable Notes in January 2025. 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 including through repayment of the Exchangeable Notes in January 2025.

Our expenses will also increase substantially if and as we:

- complete work to support a potential resubmission of our NDA for oral sulopenem;
- initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates and/or may be conducted in response to the CRL;
- establish sales, marketing and distribution capabilities either directly or through a third-party, to commercialize oral sulopenem and/or sulopenem in the United States if we obtain marketing approval from the FDA;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of oral sulopenem and/or sulopenem, 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 timing and costs of our clinical trials of oral sulopenem and sulopenem, including any clinical trials or non-clinical studies which may be required for regulatory approval of our product candidates;
- any other activities that may be required in connection with the potential resubmission of the NDA for oral sulopenem;
- the timing of regulatory filings including a potential resubmission of the NDA for oral sulopenem;

- the timing of regulatory review and potential approval of any product candidates, including oral sulopenem for the treatment of uUTI;
- 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 commercialization activities for oral sulopenem and/or sulopenem and other product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the receipt of marketing approval and revenue received from any potential commercial sales of oral sulopenem and/or sulopenem;
- the terms and timing of any future collaborations, licensing or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to an exclusive license agreement with Pfizer Inc. (Pfizer) (the Pfizer License) or other future license agreements;
- the amount and timing of any payments we may be required to make in connection with the RLNs and the repayment of the Exchangeable Notes;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;
- the costs of operating as a public company;
- 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, any potential economic slowdown or recession, including trade wars or civil or political unrest (such as the ongoing conflicts between Ukraine and Russia and Israel and Gaza) 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. Additionally, in the event we are not able to obtain shareholder approval for the disapplication of pre-emption rights over our ordinary shares at a general meeting of the shareholders, our ability to raise additional capital through the issue of new shares for cash will be severely limited. 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, the Exchangeable Notes 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 stakeholders while prudently managing our remaining resources.

Contractual Obligations and Commitments

Under the Pfizer License, we have agreed to make certain regulatory and sales milestone payments and are obligated to make a potential one-time payment related to sublicensing income that exceeds a certain threshold. We are obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage based on marginal net sales of each licensed product.

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), determined based on which of the specified sulopenem products have received FDA approval. The Payment Rate will be based on the maximum aggregate principal amount of RLNs and will equal (i) up to 15% if we or one of our affiliates has received FDA approval for the use of specified sulopenem products for the treatment of uUTIs and (ii) up to 20% if we or one of our affiliates has received FDA approval for the use of specified sulopenem products for the treatment of cUTIs but has not received FDA approval for treatment of uUTIs. There was no payment due for each of the Payment Measuring Periods through the payment measuring period ending December 31, 2023. 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 and commercial property, 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, 2023 are $0.3 million, and future contractual payments on operating lease obligations due greater than one year from December 31, 2023 are $0.1 million.

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 is disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

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

As of December 31, 2023, we had cash, cash equivalents and short-term investments of $23.9 million, consisting of cash, money market funds, commercial paper and U.S. treasury and agency bills. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. We are exposed to interest rate risk in connection with our investments in marketable securities. As interest rates change, the unrealized gains and losses associated with those securities will fluctuate accordingly. An immediate interest rate increase of 100 basis points would result in a decrease of $0.03 million in the fair market value of our portfolio as of December 31, 2023. Such losses would only be realized if we sold the investments prior to maturity.

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, 2023 and 2022, 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, 2023 and 2022. We do not currently engage in any hedging activities against our foreign currency exchange rate risk.

Item 8. Financial Statements and Supplementary Data.

ITERUM THERAPEUTICS PLC

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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, 2023 and 2022, 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, 2023, 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, 2023 and 2022, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

Going Concern

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

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 matters communicated below are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate 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 critical audit matters 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 matters below, providing separate opinions on the critical audit matters 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 $7.5 million as at December 31, 2023. The RLN liability is carried at fair value on the consolidated balance sheets and determined using a discounted cash flow (DCF) analysis. There is a degree of subjectivity in the assumptions used in the model to determine the fair value of the RLN, in particular, the discount rate, and estimated sales.

We identified the evaluation of the fair value of the RLN liability as a critical audit matter. Subjective auditor judgment, skills and knowledge were required in assessing the key assumptions used in the DCF analysis to estimate the fair values of the RLN. Minor changes to these assumptions would have a material impact on the estimated fair value.

The following are the primary procedures we performed to address this critical audit matter:

- We obtained an understanding of the client's valuation process and the design and implementation of the controls over the inputs and assumptions applied in this process.
- We assessed the Group's significant assumptions used in the DCF model to determine the fair value of the RLN liability.
- We evaluated the reasonableness of the above key assumptions by comparing those assumptions 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 ranges that were independently developed using publicly available market data for comparable entities.
- We performed sensitivity analysis on the fair value based on changes to the discount rate.
- We evaluated that all required disclosures have been included in the Form 10-K.

s/ KPMG

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

Dublin, Ireland
March 28, 2024

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

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 6,071	$ 21,092
Short-term investments	17,859	39,712
Prepaid expenses and other current assets	1,628	1,338
Income taxes receivable	38	302
Total current assets	25,596	62,444
Intangible asset, net	—	1,719
Property and equipment, net	51	69
Restricted cash	34	34
Other assets	578	2,567
Total assets	$ 26,259	$ 66,833
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 4,996	$ 2,774
Accrued expenses	7,761	4,346
Derivative liability	—	196
Other current liabilities	761	1,748
Total current liabilities	13,518	9,064
Long-term debt	11,453	10,094
Royalty-linked notes	7,503	18,372
Other liabilities	188	1,304
Total liabilities	$ 32,662	$ 38,834
Commitments and contingencies *(Note 15)*		
Shareholders' (deficit) / equity		
Undesignated preferred shares, $0.01 par value per share: 100,000,000 shares authorized at December 31, 2023 and December 31, 2022; no shares issued at December 31, 2023 and December 31, 2022	—	—
Ordinary shares, $0.01 par value per share: 80,000,000 shares authorized at December 31, 2023; 20,000,000 shares authorized at December 31, 2022, 13,499,003 shares issued at December 31, 2023; 12,598,641 shares issued at December 31, 2022	135	126
Additional paid-in capital	454,759	451,150
Accumulated deficit	(461,298)	(422,927)
Accumulated other comprehensive gain / (loss)	1	(350)
Total shareholders' (deficit) / equity	(6,403)	27,999
Total liabilities and shareholders' (deficit) / equity	$ 26,259	$ 66,833

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,		
	2023	**2022**	**2021**
Operating expenses:			
Research and development	$ (39,992)	$ (17,617)	$ (10,712)
General and administrative	(7,476)	(12,766)	(13,825)
Total operating expenses	(47,468)	(30,383)	(24,537)
Operating loss	(47,468)	(30,383)	(24,537)
Interest expense, net	(1,428)	(2,361)	(5,553)
Adjustments to fair value of derivatives	11,056	5,458	(60,964)
Cancellation of share options	—	(17,350)	—
Other income, net	82	503	195
Total other expense / (income)	9,710	(13,750)	(66,322)
Loss before income taxes	(37,758)	(44,133)	(90,859)
Income tax expense	(613)	(301)	(705)
Net loss	$ (38,371)	$ (44,434)	$ (91,564)
Net loss per share – basic and diluted	$ (2.96)	$ (3.63)	$ (8.41)
Weighted average ordinary shares outstanding – basic and diluted	12,962,362	12,236,607	10,891,178
Statements of Comprehensive Loss			
Net loss	$ (38,371)	$ (44,434)	$ (91,564)
Other comprehensive income / (loss):			
Unrealized income / (loss) on marketable securities	351	(350)	—
Comprehensive loss	$ (38,020)	$ (44,784)	$ (91,564)

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			
	Shares	Amount	Paid in Capital	Accumulated Deficit	Accumulated Other Comprehensive Gain / (Loss)	Total
Balance at December 31, 2020	3,295,402	$ 33	$ 236,337	$ (286,929)	$ —	$ (50,559)
Issuance of ordinary shares, net	3,879,300	39	68,123	—	—	68,162
Share-based compensation expense	—	—	4,319	—	—	4,319
Issuance of warrants for ordinary shares	—	—	6,199	—	—	6,199
Exercise of warrants for ordinary shares	1,417,761	14	15,275	—	—	15,289
Issuance of ordinary shares on conversion of exchangeable notes	3,592,556	36	98,352	—	—	98,388
Net loss	—	—	—	(91,564)	—	(91,564)
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)

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,		
	2023	2022	2021
Cash flows from operating activities:			
Net loss	$ (38,371)	$ (44,434)	$ (91,564)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation	31	84	391
Amortization	1,719	1,716	1,713
Lease termination adjustments	473	—	—
Share-based compensation expense	784	4,758	4,319
Cancellation of share options expense	—	17,350	—
Amortization of short-term investments	(1,145)	(183)	636
Interest on short-term investments	55	(55)	(290)
Amortization of debt discount and deferred financing costs	2,339	2,338	4,097
Interest on exchangeable notes - non-cash	811	819	1,078
Adjustments to fair value of derivatives	(11,056)	(5,458)	60,964
Other	2,267	2,281	3,254
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(3,188)	(1,551)	1,008
Other assets	322	—	(8)
Accounts payable	2,223	1,895	63
Accrued expenses	3,489	3,185	(662)
Income taxes	271	(510)	271
Other liabilities	(354)	(708)	(1,112)
Net cash used in operating activities	(39,330)	(18,473)	(15,842)
Cash flows from investing activities:			
Purchases of property and equipment	(13)	(62)	(61)
Purchases of short-term investments	(41,179)	(45,708)	(67,034)
Proceeds from sale of short-term investments	64,528	59,727	12,500
Net cash provided by / (used in) investing activities	23,336	13,957	(54,595)
Cash flows from financing activities:			
Repayments of long-term debt	—	(2,251)	(6,516)
Proceeds from issuance of ordinary shares, net of transaction costs	1,034	433	89,643
Net cash provided by / (used in) financing activities	1,034	(1,818)	83,127
Effect of exchange rates on cash and cash equivalents	(61)	(50)	4
Net (decrease) / increase in cash, cash equivalents and restricted cash	(15,021)	(6,384)	12,694
Cash, cash equivalents and restricted cash, at beginning of period	21,126	27,510	14,816
Cash, cash equivalents and restricted cash, at end of period	$ 6,105	$ 21,126	$ 27,510
Supplemental Disclosure of Cash Flow Information:			
Income tax paid—U.S.	$ 401	$ 821	$ 435
Interest paid	—	22	416

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

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

(1) Nature of Operations and Basis of Presentation

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 Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, Ireland. The Company commenced operations in November 2015. The Company licensed global rights to its novel anti-infective compound, sulopenem, from Pfizer Inc. (Pfizer). The Company is a clinical-stage pharmaceutical company dedicated to developing and commercializing sulopenem to be potentially the first oral penem available in the United States and the first and only oral and intravenous (IV) branded penem available globally.

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 (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). 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 achieve regulatory approval, failure to successfully develop and commercialize its product candidates, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology and compliance with government regulations. Product candidates currently under development will require additional research and development efforts, including regulatory approval prior to commercialization.

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

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP) and include the accounts of the Company and its subsidiaries. Certain reclassifications have been made to prior period amounts to conform with the current period's presentation, including in connection with the application of the hierarchy for fair value measurements of short-term investments, and the classification, amortised cost and unrealized gains and losses of short-term investments.

The Company's shareholders approved a reverse share split of the Company's ordinary shares on June 15, 2022, which became effective on August 17, 2022, (the Reverse Share Split). As of 5:00 p.m. Eastern Standard Time on August 17, 2022, every fifteen ordinary shares of $0.01 each (nominal value) in the authorized and unissued and authorized and issued share capital of the Company were consolidated into one ordinary share of $0.15 each (nominal value), and the nominal value of each ordinary share was subsequently reduced from $0.15 to $0.01 nominal value per share. No fractional shares were issued to any shareholders in connection with the Reverse Share Split. Shareholders who were otherwise entitled to receive a fractional ordinary share instead received a cash payment in an amount equal to the net cash proceeds attributable to the sale of such fractional entitlement following aggregation and sale by the Company on behalf of each of the relevant shareholders of the Company's ordinary shares, on the basis of prevailing market prices at such time. As the par value per share of the Company's shares remained at $0.01 per share following the Reverse Share Split, the difference between the total share capital at (par value) prior to the Reverse Share Split and the total share capital (par value) after the Reverse Share Split, has been reclassified as additional paid-in-capital on a retroactive basis. The number of ordinary shares reserved for issuance upon exercise of the Exchangeable Notes, outstanding share options and warrants or upon the vesting of outstanding restricted share units, was adjusted and proportionately decreased and the exercise price of all share options, Exchangeable Notes and warrants was proportionately increased. Additionally, the number of shares that may be the subject of future grants under our share plans was proportionally decreased. Accordingly, all historical share and per share information related to the issued and outstanding ordinary shares, the Exchangeable Notes, share options, restricted share units, warrants and shares reserved for future issuance under the Company's share plans have been adjusted to reflect the Reverse Share Split for all prior periods presented.

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 H.C. Wainwright & Co., LLC (HC Wainwright), as agent, pursuant to which the Company may offer and sell ordinary shares, nominal value $0.01 per share, 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.

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 $38,371, $44,434 and $91,564 for the years ended December 31, 2023, 2022 and 2021, respectively. The Company had an accumulated deficit of $461,298 as of December 31, 2023 and expects to continue to incur net losses for the foreseeable future. The Company's future cash flows are dependent on key variables such as its ability to secure additional sources of funding in the form of public or private financing of debt or equity or collaboration agreements. Based on its available cash, cash equivalents and short-term investments, including amounts raised subsequent to the year end under the "at-the-market" agreement, as disclosed in Note 17 − Subsequent Events, 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 including the repayment of the Exchangeable Notes in January 2025. 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 H.C. 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, the Company's ability to raise additional capital through the issue of new shares for cash is limited to issuing only 1.8 million ordinary shares (or rights to acquire such shares) for cash, based on the amount of authorized ordinary shares unissued or unreserved and free from any statutory rights of pre-emption, and therefore available for issuance as of February 29, 2024. While shareholders approved an increase of an additional 60,000,000 ordinary shares at our annual general meeting in May 2023 (the Additional Shares), we did not receive approval for the disapplication of statutory pre-emption rights over such shares. Absent shareholder approval of the dis-application of statutory pre-emption rights with respect to the Additional Shares, any Additional Shares that we propose to issue for cash will first have to be offered to all of our existing shareholders on the same or more favorable terms on a pro-rata basis. As a result of this limitation, we are currently severely limited in the amount of ordinary shares we may sell for cash in any capital raising transaction, and where we propose to issue shares for cash consideration, we may be required to first offer those shares to all of our existing shareholders in a time-consuming pro-rata rights offering. Furthermore, while the statutory pre-emption right applies only to share issuances for cash consideration and it does not apply where we issue shares for non-cash consideration (such as in a share exchange transaction or in any transaction in which property other than cash is received by us in payment for shares), any such transaction would likely be time-consuming and complex to execute. In addition, in parallel, the Company is evaluating its corporate, strategic, financial and financing alternatives, with the goal of maximizing value for its stakeholders. 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 and the reported amounts of expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the valuation of share-based compensation awards, the valuation of the RLNs and the Derivative liabilities, which consist of embedded features in the Exchangeable Notes, and the accrual for research and development expenses. 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 discounted cash flow analysis (DCF) 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 stockholders' equity that result from transactions and economic events other than those with shareholders. For the years ended December 31, 2023 and 2022, 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, 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 consist 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 stockholders' (deficit) / 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 $110 (€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, 2023 and 2022, 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, 2023 and 2022, 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, 2023 and 2022, 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 asset was stated at cost less accumulated amortization. The Company calculated amortization expense using the straight-line method over the estimated useful life of the related asset which the Company believed reasonably represented the time period in which the economic benefit of the intangible asset was consumed or otherwise realized. The Company reviewed the recoverability of the finite-lived intangible asset and, when there were indications that this asset was 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, or CROs, and investigative sites in connection with preclinical studies and clinical trials; and
- Contract Manufacturing Organizations, or CMOs, in connection with drug substance and drug product formulation of preclinical and clinical trial materials.

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

Patent Costs

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

Share-Based Compensation

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

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

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

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

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

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

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

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

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, 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.

In determining the appropriate fair values, the Company used the binomial option pricing model, and in the case of the change of control component, in combination with a DCF analysis, which is discussed in Note 3 – Fair Value of Financial Assets and Liabilities. The Company's derivative financial instruments consisted of embedded features in the Exchangeable Notes. The embedded derivatives include provisions that provide the noteholder with certain exchange rights and protections on a fundamental change such as a change of control. The effects of interactions between embedded derivatives are calculated and accounted for in arriving at the overall fair value of the financial instruments.

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 provision 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.

Concentration of Credit Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and short-term investments. The Company has most of its cash, cash equivalents and short-term investments 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.

(In thousands, except share and per share data)

	Year ended December 31,		
	2023	2022	2021
Options to purchase ordinary shares	1,109,654	355,591	1,068,639
Unvested restricted share units	16,666	128,728	119,017
Warrants	480,186	480,186	480,186
Exchangeable Notes	1,255,451	1,287,660	1,217,386
Total	2,861,957	2,252,165	2,885,228

Segment and Other Information

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

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

	Year ended December 31,		
Operating expenses	2023	2022	2021
Ireland	$ 41,829	$ 22,015	$ 15,926
U.S.	5,603	8,332	8,554
Bermuda	36	36	57
Total	$ 47,468	$ 30,383	$ 24,537

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

Long lived assets	December 31, 2023	December 31, 2022
Ireland	$ 342	$ 4,052
U.S.	287	303
Total	$ 629	$ 4,355

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, 2023 and 2022 of $0.03 million and $0.02 million, respectively. No top-heavy contribution was required to be made for the year ended December 31, 2021.

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, 2023 or December 31, 2022.

(In thousands, except share and per share data)

Contingent Consideration

Certain license agreements contain milestone payments that could result in the requirement to make contingent consideration payments, see Note 15 for further details. Contingent consideration is recorded at the acquisition date estimated fair value of the contingent payment. The fair value of the contingent consideration is measured at each reporting period. Any related unwinding of discount is recognized as a finance expense. Other changes in fair value are recognized in profit or loss or capitalized as an intangible asset depending on the stage of development. As of December 31, 2023, no milestones had been met that required the Company to recognize contingent consideration.

Recently Adopted Accounting Pronouncements

In June 2016 the FASB issued ASU No. 2016-13, Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments, or ASU 2016-13. The FASB subsequently issued amendments to ASU 2016-13, which have the same effective date and transition date of January 1, 2023. These standards require that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, these standards now require allowances to be recorded instead of reducing the amortized cost of the investment. These standards limit the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and requires the reversal of previously recognized credit losses if fair value increases. The new standard became effective for the Company on January 1, 2023 and did not have a material impact on the Company's consolidated financial statements.

Recent Accounting Pronouncements

On November 27, 2023, the FASB issued ASU No. 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures, or* ASU No. 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 thereafter. Early adoption is permitted. ASU 2023-07 is not expected to have a material impact on the consolidated financial statements.

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, or* 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.

(3) Fair Value of Financial Assets and Liabilities

The following table presents information about the Company's financial assets that were carried at fair value on a recurring basis on the consolidated balance sheet as of December 31, 2023 and December 31, 2022 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	$ —

December 31, 2022 **Assets**	**Total**	**Level 1**	**Level 2**	**Level 3**
Short-term investments:				
Corporate bonds	$ 7,781	$ —	$ 7,781	$ —
Commercial paper	15,232	—	15,232	—
U.S. Treasury bonds	16,699	—	16,699	—
	$ 39,712	$ —	$ 39,712	$ —

(In thousands, except share and per share data)

See Note 4 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 debt, Exchangeable Notes, Derivative liability and RLNs and indicates the fair value hierarchy of the valuation inputs utilized to determine the approximate fair value:

December 31, 2023

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

December 31, 2022

Liabilities	Book Value	Approximate Fair Value	Level 1	Level 2	Level 3
Exchangeable Notes					
Long-term exchangeable notes	$ 10,094	$ 10,827	$ —	$ 10,827	$ —
Derivative liability - exchange option and change of control	196	196	—	—	196
Revenue Futures					
Royalty-linked notes	18,372	18,372	—	—	18,372
Total	$ 28,662	$ 29,395	$ —	$ 10,827	$ 18,568

The fair value of long-term 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 Level 3 liabilities held as of December 31, 2023 consist of a separate financial instrument, that was issued as part of the Units, the RLNs (see Note 11 – Royalty-Linked Notes). The Level 3 liabilities held as of December 31, 2022 consist of the embedded exchange option and change of control premium contained in the Exchangeable Notes (see Note 10 - Debt) and a separate financial instrument, that was issued as part of the Units, the RLNs (see Note 11 - Royalty-Linked Notes). The exchange option and change of control premium met the criteria requiring these to be bifurcated and accounted for separately from the host debt in accordance with ASC 815-15, *Derivatives and Hedging; Embedded Derivatives*. The exchange option and change of control premium were presented as a Derivative liability upon issuance of the Exchangeable Notes under the Private Placement and Rights Offering and are subsequently remeasured to fair value at the end of each reporting period. The fair value of the exchange option and change of control premium at December 31, 2023 were $0. 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 89.9035 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an exchange price of approximately $11.123 per ordinary share) as of December 31, 2023, 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, 2023, 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, 2023 was $11,117.

In the event of a fundamental change that is not a liquidation event (Fundamental Change), under the Exchangeable Notes Indenture, the Company will be required to pay each holder of an Exchangeable Note 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 Derivative liability, representing the change of control feature, was recorded at a fair value of $0 at December 31, 2023.

The fair value of each component of the Derivative liability was determined using the binomial option pricing model, and in the case of the change of control component, in combination with a DCF analysis, without consideration of transaction costs, which represents a Level 3 basis of fair value measurement. The key inputs to valuing the Derivative liability as of December 31, 2023 include the terms of the Exchangeable Notes Indenture, the Company's share price and market capitalization, the expected annual

(In thousands, except share and per share data)

volatility of the Company's ordinary shares, management's assumption regarding the probability of a Fundamental Change pursuant to the terms of the Exchangeable Notes Indenture, and the risk-free interest rate. 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.

The following table presents the changes in fair value of the Company's Derivative liability:

	2023	2022
Balance at January 1	$ 196	$ 6,058
Conversion of Exchangeable Notes	(9)	—
Adjustment to fair value	(187)	(5,862)
Balance at December 31	$ —	$ 196

The following summary table shows the assumptions used in the binomial option pricing model to estimate the fair value of the exchange option:

	December 31, 2023	December 31, 2022
Share price	$1.97	$0.84
Market capitalization	$26,593,036	$10,582,858
Volatility	100%	100%
Risk-free interest rate	4.20%	4.46%
Dividend rate	0%	0%

The additional significant assumption used in the DCF model to estimate the fair value of the change of control feature at December 31, 2023 was management's assumption regarding the probability of a Fundamental Change pursuant to the terms of the Exchangeable Notes Indenture.

The RLN liability is carried at fair value on the consolidated balance sheet (see Note 11 – Royalty-Linked Notes). The total fair value of $7,503 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 risk-adjusted 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, 2023 and 2022. 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 as at year end consist of corporate bonds, commercial paper and U.S. Treasury bonds with maturities of more than three months at the date of purchase. Short-term investments as of December 31, 2023 have a weighted average maturity of 0.15 years. The investments are reported at fair value with unrealized gains or losses recorded in the consolidated statements of operations and comprehensive loss. Any differences between the 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 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	$ —

(In thousands, except share and per share data)

The following table represents the Company's available for sale short-term investments by major security type as of December 31, 2022:

December 31, 2022					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	$ 7,836	$ —	$ (55)	$ 7,781	$ 7,781	$ —
Commercial paper	15,230	2	—	15,232	15,232	—
U.S. Treasury bonds	16,996	—	(297)	16,699	16,699	—
Total	$ 40,062	$ 2	$ (352)	$ 39,712	$ 39,712	$ —

(5) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following:

	December 31, 2023	December 31, 2022
Prepaid research and development expenses	$ 872	$ 458
Prepaid insurance	472	592
Research and development tax credit receivable	195	118
Other prepaid assets	89	170
Total	$ 1,628	$ 1,338

(6) Intangible Asset, net

Intangible asset and related accumulated amortization are as follows:

	December 31, 2023	December 31, 2022
Gross intangible asset	$ 5,148	$ 5,148
Less: accumulated amortization	(5,148)	(3,429)
	$ —	$ 1,719

On December 10, 2021, the Company entered into an amendment to an agreement with a supplier whereby advance payments made from June 2016 to January 2020 were being set against a reservation fee for a tableting facility for the period from January 1, 2021 to December 31, 2023. This reservation right was amortized over the three year term of the amended agreement.

(7) Property and Equipment, net

Property and equipment and related accumulated depreciation are as follows:

	December 31, 2023	December 31, 2022
Leasehold improvements	$ 148	$ 148
Furniture and fixtures	120	120
Computer equipment	98	85
	366	353
Less: accumulated depreciation	(315)	(284)
	$ 51	$ 69

Depreciation expense was $31, $84 and $391 for the years ended December 31, 2023, 2022 and 2021, respectively.

(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 1.16 years to 1.59 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. The renewal option on another lease was derecognized in June 2022 as it was no longer reasonably certain that the option would be exercised, resulting in a reduction in the remaining term from 16 to six years. A Deed of Assignment was signed in August 2023 in relation to this 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 thousands, except share and per share data)

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 extend more than 12 months from the end of the previously determined lease term, it is considered to be reasonably certain that these lease arrangements will be extended beyond a period of more than 12 months. Accordingly, the Company has applied the measurement and recognition requirements of ASC 842 to these lease arrangements.

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 $363, $753 and $1,009 of operating lease costs for right-of-use assets during the years ended December 31, 2023, 2022 and 2021, respectively. The Company recognized $194 and $243 of rental expenses on short-term leases during the years ended December 31, 2023 and 2022, respectively. The Company recognized $199, $293 and $335 of sublease income during the years ended December 31, 2023, 2022 and 2021, respectively.

Information related to the Company's right-of-use assets and related lease liabilities is as follows:

	December 31, 2023	December 31, 2022
Cash paid for operating lease liabilities	$ 354	$ 709

	December 31, 2023	December 31, 2022
Weighted-average remaining lease term	1.46 years	5.04 years
Weighted-average discount rate	12.9%	5.5%

Right-of-use assets and lease liabilities for the Company's operating leases were recorded in the consolidated balance sheet as follows, representing the Company's right to use the underlying asset for the lease term ("Other assets") and the Company's obligation to make lease payments ("Other current liabilities" and "Other liabilities"):

	December 31, 2023	December 31, 2022
Other assets	$ 549	$ 1,770
Other current liabilities	$ 365	$ 332
Other liabilities	188	1,304
Total lease liabilities	$ 553	$ 1,636

Future lease payments included in the measurement of lease liabilities on the consolidated balance sheet as of December 31, 2023 for the following five fiscal years and thereafter were as follows:

(In thousands, except share and per share data)

Due in 12 month period ended December 31,	
2024	$ 405
2025	197
2026	—
2027	—
2028	—
Thereafter	—
	$ 602
Less imputed interest	(49)
Total lease liabilities	$ 553

(9) Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2023	December 31, 2022
Accrued clinical trial costs	$ 4,835	$ 1,549
Accrued payroll and bonus expenses	2,742	1,971
Accrued other expenses	147	220
Accrued professional fees	37	606
Total	$ 7,761	$ 4,346

(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 and $556 of interest expense related to the Loan and Security Agreement during the years ended December 31, 2022 and 2021, respectively, including $6 and $142 related to the accretion of the debt discounts and deferred financing costs during the years ended December 31, 2022 and 2021, respectively. 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 89.9035 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an exchange price of approximately $11.123 per ordinary share) as of December 31, 2023, 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, 2023, 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, 2023 was $11,117.

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 $811, $820 and $1,078 of interest expense related to the Exchangeable Notes during the years ended December 31, 2023, 2022 and 2021, respectively, and $2,339, $2,344 and $2,893 related to the amortization of the debt discounts and deferred financing costs during the years ended December 31, 2023, 2022 and 2021, respectively. These amounts are recorded in interest expense, net in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2023, 2022 and 2021, respectively. The balance of the Exchangeable Notes at each reporting date is as follows:

(In thousands, except share and per share data)

	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

	December 31, 2022	
	Principal	Accrued Interest
January 2020 $1,000 Exchangeable Notes, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	$ 51,588	$ 5,058
September 2020 $1,000 Exchangeable Notes, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	220	20
Conversion of $1,000 Exchangeable Notes, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	(39,201)	(2,697)
2025 Exchangeable Notes	12,607	2,381
Unamortized discount and debt issuance costs	(4,894)	—
2025 Exchangeable Notes, net	$ 7,713	$ 2,381

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 and $309 were made during the years ended December 31, 2022 and 2021, respectively. The Company recognized $0 and $2 of interest expense related to the loan agreement during the years ended December 31, 2022 and 2021, respectively. All outstanding amounts were repaid on March 17, 2022, effectively terminating the PPP loan.

Scheduled principal payments on outstanding debt, including principal amounts owed to RLN holders (see Note 11 – Royalty-Linked Notes) as of December 31, 2023, for the following five fiscal years and thereafter were as follows:

Year Ending December 31,	
2024	$ —
2025	11,117
2026	—
2027	—
2028	—
Thereafter	104
	$ 11,221

(In thousands, except share and per share data)

(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 (or December 31, 2025, in the event that the Company has not yet received FDA approval with respect to one or more specified sulopenem products by such date), 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 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, *Debt*. 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 non-cash adjustment of $11,056 during the year ended December 31, 2023, to the fair value of the RLN were primarily a result of the reduction in management's forecasted U.S. sulopenem sales. 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, 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

	December 31, 2022
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	3,665
Total liability related to the sale of future royalties at December 31, 2022	$ 18,372
Current Portion	—
Long-term Portion	$ 18,372

(12) 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

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, 2023. The holders of ordinary shares are entitled to one vote for each share held. The holders of ordinary shares currently have preemptive rights over 60,000,000 ordinary shares and no preemptive or other subscription rights over 20,000,000 ordinary shares. 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, the Company entered into a sales agreement with HC Wainwright, as agent, pursuant to which the Company may offer and sell ordinary shares, nominal value $0.01 per share, 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. During the years ended December 31, 2023 and 2022, the Company sold 639,825 and 356,933 ordinary shares under the "at-the-market" agreement at an average price of $1.68 and $1.25 per share for net proceeds of $1.0 million and $0.4 million, 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, 2023, 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, 2023 was $11,117.

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, 2023.

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, 2023.

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, 2023, 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, 2023, 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, 2023, 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, 2023.

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, 2023.

Undesignated Preferred Shares

The Company has authorized 100,000,000 undesignated preferred shares of $0.01 par value each as of December 31, 2023. 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, 2023 or December 31, 2022.

(13) 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 granted 857,500, 197,085 and 1,028,090 share options to employees and directors during the years ended December 31, 2023, 2022 and 2021, respectively. There were 930,010, 296,199 and 1,033,820 unvested employee and director options outstanding as of December 31, 2023, December 31, 2022 and December 31, 2021, respectively. Total expense recognized related to the employee and director share options was $468, $3,580, and $3,779, for the years ended December 31, 2023, 2022 and 2021, respectively. Total unamortized compensation expense related to employee and director share options was $1,000, $929 and $21,521 as of December 31, 2023, December 31, 2022 and December 31, 2021, respectively, expected to be recognized over a remaining weighted average vesting period of 2.09 years, 1.41 years and 3.49 years as of December 31, 2023, December 31, 2022 and December 31, 2021, 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	2021
Volatility	100%	100 - 130%	120 - 140%
Expected term in years	6.00 - 6.25	5.50 - 6.25	5.50 - 6.25
Dividend rate	0%	0%	0%
Risk-free interest rate	3.55% - 3.67%	1.90 - 3.96%	0.90 - 1.42%
Share price	$1.00 - $1.04	$0.81-$6.72	$0.48-$2.01
Fair value of option on grant date	$0.80 - $0.84	$0.64-$5.95	$0.45-$1.75

The following table summarizes total stock option activity for all Company plans:

	Equity Plans	Inducement Plan	Total
Options outstanding December 31, 2020	63,431	—	63,431
Granted	908,090	120,000	1,028,090
Exercised	—	—	—
Forfeited	—	—	—
Expired	(22,882)	—	(22,882)
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)
Options outstanding December 31, 2023	984,155	124,833	1,108,988

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, 2020	63,431	$ 110.40	5.41	—
Granted	1,028,090	$ 27.13		
Exercised	—			
Forfeited	—			
Expired	(22,882)	$ 118.49		
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	—	$ 18.76		
Options outstanding December 31, 2023	1,108,988	$ 2.73	8.94	$ 832
Exercisable at December 31, 2023	178,978	$ 9.05	7.94	—

(In thousands, except share and per share data)

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, 2023, December 31, 2022 and December 31, 2021.

The weighted average grant-date fair value per share of share options granted during the years ended December 31, 2023, 2022 and 2021 was $0.80, $2.39 and $23.67, respectively.

Restricted Share Units (RSUs)

No RSUs were granted to employees or directors during the year ended December 31, 2023. The Company granted 66,398 RSUs to directors during the year ended December 31, 2022 and 123,017 RSUs to employees and directors during the year ended December 31, 2021.

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, 2020	—	—	—
Granted	89,684	33,333	123,017
Shares vested	(4,000)	—	(4,000)
Forfeited	—	—	—
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

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, 2020	—	
Granted	123,017	$ 19.32
Shares vested	(4,000)	$ 24.00
Forfeited	—	
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

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 expense recognized related to the RSUs was $316, $1,178 and $960 for the years ended December 31, 2023, 2022 and 2021, respectively. Total unamortized

(In thousands, except share and per share data)

compensation expense related to the RSUs was $116, $434 and $1,416 as of December 31, 2023, 2022 and 2021, respectively, and is expected to be recognized over a remaining average vesting period of 1.92 years, 0.88 years and 1.89 years as of December 31, 2023, December 31, 2022 and December 31, 2021, respectively.

No RSUs, which are subject to certain performance-based vesting conditions (Performance RSUs), were awarded during the years ended December 31, 2023, 2022 and 2021.

The table below shows the number of Performance RSUs granted covering an equal number of the Company's ordinary shares and the weighted-average grant date fair value of the Performance RSUs granted:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Performance RSUs outstanding December 31, 2020	65,527	$ 33.18
Granted	—	
Shares vested	(41,961)	$ 30.90
Expired	(1,733)	$ 29.85
Forfeited	(21,833)	$ 123.15
Performance RSUs outstanding December 31, 2021	—	

The weighted average grant date fair value of Performance RSUs with a market condition was determined using the Monte Carlo simulation model. The fair value of Performance RSUs is expensed ratably over the vesting period. Due to the expiration of Performance RSUs, a credit of $420 was recognized for the year ended December 31, 2021. All Performance RSUs were fully expensed as of December 31, 2021.

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

	Year ended December 31,		
	2023	2022	2021
Research and development expense	$ 412	$ 1,396	$ 1,322
General and administrative expense	372	3,362	2,997

There was a total of $1,116, $1,363 and $22,937 unamortized share-based compensation expense for share options and restricted share units as of December 31, 2023, December 31, 2022 and December 31, 2021, respectively, expected to be recognized over a remaining average vesting period of 2.07 years, 1.28 years and 3.32 years as of December 31, 2023, December 31, 2022 and December 31, 2021, respectively.

(14) Income Taxes

During the years ended December 31, 2023, 2022 and 2021, 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,		
	2023	2022	2021
Current			
U.S.	$ 613	$ 301	$ 705
Ireland	—	—	—
Total Current	$ 613	$ 301	$ 705
Deferred			
U.S.	$ —	$ —	$ —
Ireland	—	—	—
Total Deferred	$ —	$ —	$ —
Income Tax Provision	$ 613	$ 301	$ 705

(In thousands, except share and per share data)

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

	Year Ended December 31,		
	2023	2022	2021
U.S.	$ 1,743	$ (13,701)	$ (34)
Ireland	(39,501)	(30,432)	(90,825)
Total	$ (37,758)	$ (44,133)	$ (90,859)

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

	Year Ended December 31, 2023		Year Ended December 31, 2022		Year Ended December 31, 2021	
Statutory rate	12.50%	$ (4,720)	12.50%	$ (5,517)	12.50%	$ (11,357)
Impact of U.S. tax rate	0.72%	(272)	4.71%	(2,080)	0.01%	(5)
Impact of valuation allowance	(14.48)%	5,466	(5.30)%	2,341	(3.64)%	3,304
Research and development tax credit	0.00%	—	0.00%	—	0.00%	—
Adjustments for current tax of prior periods	0.14%	(52)	(4.19)%	1,851	0.14%	(131)
Cancellation of share options	0.00%	—	(9.02)%	3,983	0.00%	—
Fair value movements on derivative financial instruments	3.66%	(1,382)	1.55%	(682)	(8.37)%	7,603
Other, net	(4.17)%	1,573	(0.92)%	405	(1.42)%	1,292
Effective tax rate	(1.62)%	$ 613	(0.68)%	$ 301	(0.78)%	$ 705

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

	Year Ended December 31,		
	2023	2022	2021
Deferred tax assets			
Share-based compensation	$ 154	$ 438	$ 822
Depreciation	45	42	127
Net operating loss carryforwards	41,525	36,059	33,218
Other	4	(11)	120
Valuation allowance	(41,728)	(36,528)	(34,287)
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 $41,525, $36,059 and $33,218 as of the years ended December 31, 2023, 2022 and 2021, 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.

(In thousands, except share and per share data)

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

	2023	2022
Balance at January 1	$ 2,844	$ 3,300
Decrease in tax positions	(824)	(456)
Balance at December 31	$ 2,020	$ 2,844

The Company's federal and state income tax returns for 2020 through 2022 remain open to examination by the IRS. The Company's income tax returns in Ireland remain open to examination from 2019 to 2022. 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, 2023.

(15) Commitments and Contingencies

License Agreement

On November 18, 2015, the Company entered into a license agreement with Pfizer for the worldwide exclusive rights to research, develop, manufacture and commercialize sulopenem.

As part of the license agreement, the Company is obligated to pay Pfizer potential future regulatory milestone payments, as well as sales milestones upon achievement of net sales ranging from $250.0 million to $1.0 billion for each product type. The Company is also obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage based on marginal net sales of each licensed product.

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 (or December 31, 2025, in the event that the Company has not yet received FDA approval with respect to one or more specified sulopenem products by such date), 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.

(16) 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, 2023, $11,117 aggregate principal amount of Exchangeable Notes and all RLNs remained outstanding.

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.

(17) Subsequent Events

Extraordinary General Meeting of Shareholders

On January 30, 2024, the Company asked its shareholders to renew the disapplication of statutory pre-emption rights over 5,000,000 authorized but unissued ordinary shares at an extraordinary general meeting of shareholders. Although the Company received over 53% support of the votes cast on renewing the disapplication of statutory pre-emption rights at the EGM, the Company did not receive the affirmative vote of at least 75% of the votes cast as required under Irish law for the passing of special resolutions.

Data readout - Phase 3 clinical trial for oral sulopenem for the treatment of uncomplicated urinary tract infections

In January 2024, the Company announced that sulopenem 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.

Equity Offerings

Subsequent to December 31, 2023, through February 29, 2024, the Company sold 2.9 million ordinary shares under the "at-the-market" agreement, with HC Wainwright as agent, at an average price of $2.52 per share for net proceeds of $7.1 million.

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, 2023. 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, 2023, 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, 2023.

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, 2023, 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, 2023, our Chief Medical Officer Dr. Puttagunta terminated an instruction for the sale of securities that was intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) of the Exchange Act or any non-Rule 10b5-1 trading arrangement (as defined in the Securities and Exchange Commission's rules). The automatic sale instructions were executed by Dr. Puttagunta on December 12, 2021 in connection with the grant of 33,333 restricted share units vesting over four years, with 25% of the restricted share units fully vesting on each one-year anniversary of December 1, 2021 (the "RSU Grant"). The

automatic sale instructions covered such number of ordinary shares issuable with respect to the restricted share units vesting on each relevant vesting date as was sufficient to generate net proceeds sufficient to satisfy the Company's minimum statutory withholding obligations with respect to the income recognized by Dr. Puttagunta upon the vesting of such restricted share units (based on minimum statutory withholding rates for all tax purposes, including payroll and social taxes, applicable to such income). The termination covered the automatic sale instructions given with respect to 24,999 restricted share units included in the RSU Grant vesting over the remaining 3 year vesting period, on December 1, 2023, December 1, 2024 and December 1, 2025.

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.

The information required by this item is incorporated herein by reference to the information in our definitive Proxy Statement to be filed in connection with our 2024 Annual General Meeting of Shareholders (2024 Proxy Statement), which will be filed with the Securities and Exchange Commission within 120 days after December 31, 2023.

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.

Item 11. Executive Compensation.

The information required by this item is incorporated herein by reference to our 2024 Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters.

The information required by this item is incorporated herein by reference to our 2024 Proxy Statement.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item is incorporated herein by reference to our 2024 Proxy Statement.

Item 14. Principal Accounting Fees and Services.

The information required by this item is incorporated herein by reference to our 2024 Proxy Statement.

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	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	X			
10.21+	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
10.22+	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
10.23+	Amended and Restated Non-Employee Director Compensation Policy		Form 8-K (Exhibit 10.1)	March 16, 2021	001-38503
10.24	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
10.25	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
10.26	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
10.27	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
10.28	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

10.29	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
10.30	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
10.31	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
10.32	Iterum Therapeutics plc 2021 Inducement Equity Incentive Plan, as amended		Form 10-Q (Exhibit 10.3)	November 10, 2022	001-38503
10.33	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
10.34	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
10.35	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
10.36	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
10.37	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
10.38	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
19.1	Insider Trading and Trading Window Policy	X			
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	X			
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			

+ 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: March 28, 2024

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

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ Corey N. Fishman Corey N. Fishman	President and Chief Executive Officer (Principal Executive Officer)	March 28, 2024
/s/ Judith M. Matthews Judith M. Matthews	Chief Financial Officer (Principal Financial and Accounting Officer)	March 28, 2024
/s/ Michael Dunne Michael Dunne M.D.	Director	March 28, 2024
/s/ Ronald M. Hunt Ronald M. Hunt	Director	March 28, 2024
/s/ David G. Kelly David G. Kelly	Director	March 28, 2024
/s/ Beth Hecht Beth Hecht	Director	March 28, 2024

April 26, 2024

Dear Shareholder,

You are cordially invited to the 2024 Annual General Meeting of Shareholders to be held at 3 Dublin Landings, North Wall Quay, Dublin 1, Ireland on June 19, 2024 at 3.00 p.m., Irish time (10.00 a.m., Eastern Time). The enclosed notice of Annual General Meeting of Shareholders sets forth the proposals that will be presented at the meeting, which are described in more detail in the proxy statement.

At this year's Annual General Meeting, we will ask shareholders to:

1. elect, by separate resolutions, the two nominees for Class III directors named herein, each to serve for a three-year term expiring at the 2027 annual general meeting of shareholders;
2. ratify, in a non-binding vote, the appointment of KPMG as our independent registered public accounting firm for our fiscal year ending December 31, 2024, and to authorize the board of directors, acting through the audit committee, to set the independent registered public accounting firm's remuneration;
3. approve, in a non-binding, advisory vote, named executive officer compensation;
4. recommend, in a non-binding, advisory vote, the frequency of future named executive compensation advisory votes;
5. receive and consider the Company's Irish Statutory Financial Statements for the fiscal year ended December 31, 2023 and the reports of the directors and auditors thereon, and review the affairs of the Company; and
6. consider any other business properly brought before the 2024 Annual General Meeting of Shareholders or any adjournment or postponement thereof.

Our board of directors unanimously recommends a vote "FOR" Proposal Nos. 1 and 2 as set forth in the proxy statement.

We hope that you will participate in the meeting by voting through acceptable means as described in this proxy statement as promptly as possible. Your vote is important – so please exercise your right.

Sincerely,

Corey N. Fishman
President and Chief Executive Officer

This proxy statement, the enclosed proxy card, our 2023 annual report to shareholders and our Irish Statutory Financial Statements for the fiscal year ended December 31, 2023 are being made available to shareholders on or about April 26, 2024.

ITERUM THERAPEUTICS PLC
Fitzwilliam Court, 1st Floor
Leeson Close
Dublin 2
Ireland

NOTICE OF ANNUAL GENERAL MEETING OF SHAREHOLDERS
to be held on June 19, 2024

The 2024 Annual General Meeting of Shareholders (the "AGM") of Iterum Therapeutics plc, an Irish public limited company (the "Company"), will be held on June 19, 2024, beginning at 3.00 p.m., Irish time (10.00 a.m., Eastern Time), at 3 Dublin Landings, North Wall Quay, Dublin 1, Ireland to consider and act upon the following matters:

1. To elect, by separate resolutions, the two nominees for Class III director named herein, each to serve for a three-year term expiring at the 2027 annual general meeting of shareholders.
2. To ratify, in a non-binding vote, the appointment of KPMG as our independent registered public accounting firm for our fiscal year ending December 31, 2024, and to authorize the board of directors, acting through the audit committee, to set the independent registered public accounting firm's remuneration.
3. To vote on, an advisory, non-binding, resolution to approve the compensation of our named executive officers.
4. To vote on an advisory, non-binding, proposal on the frequency of future advisory votes on the compensation of our named executive officers.
5. To receive and consider the Company's Irish Statutory Financial Statements for the fiscal year ended December 31, 2023 and the reports of the directors and auditors thereon, and to review the affairs of the Company.
6. To conduct any other business properly brought before the AGM or any adjournment or postponement thereof.

Proposal Nos. 1 and 2 above are ordinary resolutions requiring a simple majority of the votes cast at the meeting to be approved. Proposal No. 4 provides a choice among three frequency periods (every one, two or three years) for future advisory votes on the compensation of our named executive officers. If none of the three frequency options receives a simple majority of the votes cast, we will consider the frequency option (one year, two years or three years) receiving the highest number of votes cast by shareholders to be the frequency that has been recommended by our shareholders. Proposal No. 3 and Proposal No. 4 are non-binding, advisory votes, and accordingly there is no "required vote" that would constitute approval. All proposals are more fully described in this proxy statement. There is no requirement under Irish law that the Company's Irish Statutory Financial Statements for the fiscal year ended December 31, 2023, or the directors' and auditor's reports thereon be approved by the shareholders, and no such approval will be sought at the AGM.

Shareholders of record at the close of business on April 24, 2024 will be entitled to notice of and to vote at the AGM or any adjournment or postponement thereof. Instead of mailing a printed copy of our proxy materials to all of our shareholders, we provide access to these materials to many of our shareholders via the Internet, in accordance with rules adopted by the Securities and Exchange Commission. If you received only a Notice of Internet Availability of Proxy Materials, or Notice, by mail or e-mail, you will not receive a paper copy of the proxy materials unless you request one. Instead, the Notice will provide you with instructions on how to access and view the proxy materials on the Internet. The Notice will also instruct you as to how you may access your proxy card to vote online or by telephone. If you received a Notice by mail or e-mail and would like to receive a paper copy of our proxy materials, free of charge, please follow the instructions included in the Notice. The Notice is being mailed to our shareholders on or about April 26, 2024 and sent by e-mail to our shareholders who have opted for such means of delivery on or about April 26, 2024.

By order of the Board of
Directors,

Louise Barrett
Secretary

Dublin, Ireland
April 26, 2024

YOU MAY OBTAIN ADMISSION TO THE AGM BY IDENTIFYING YOURSELF AT THE AGM AS A SHAREHOLDER AS OF THE RECORD DATE. IF YOU ARE A RECORD OWNER, POSSESSION OF A COPY OF A PROXY CARD WILL BE ADEQUATE IDENTIFICATION. IF YOU ARE A BENEFICIAL (BUT NOT RECORD) OWNER, A "LEGAL PROXY" OR A COPY OF AN ACCOUNT STATEMENT FROM YOUR BANK, BROKER OR OTHER NOMINEE SHOWING SHARES HELD FOR YOUR BENEFIT ON APRIL 24, 2024 WILL BE ADEQUATE IDENTIFICATION.

WHETHER OR NOT YOU EXPECT TO ATTEND THE AGM, PLEASE SUBMIT YOUR VOTING INSTRUCTIONS VIA THE INTERNET OR BY TELEPHONE BY FOLLOWING THE INSTRUCTIONS SET FORTH ON THE ENCLOSED PROXY CARD OR, IF YOU RECEIVED A PRINTED COPY OF THE PROXY MATERIALS, BY COMPLETING, DATING AND SIGNING THE ENCLOSED PROXY CARD AND MAILING IT PROMPTLY IN THE PROVIDED ENVELOPE. TO HELP ENSURE REPRESENTATION OF YOUR SHARES AT THE AGM, NO POSTAGE NEED BE AFFIXED IF THE PROXY CARD IS MAILED IN THE UNITED STATES.

A SHAREHOLDER ENTITLED TO ATTEND AND VOTE AT THE AGM IS ENTITLED, USING THE PROXY CARD PROVIDED (OR IN THE FORM IN SECTION 184 OF THE IRISH COMPANIES ACT 2014), TO APPOINT ONE OR MORE PROXIES TO ATTEND, SPEAK AND VOTE INSTEAD OF HIM OR HER AT THE AGM. A PROXY NEED NOT BE A SHAREHOLDER OF RECORD.

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ITERUM THERAPEUTICS PLC
Fitzwilliam Court, 1st Floor
Leeson Close
Dublin 2
Ireland

PROXY STATEMENT FOR THE ANNUAL GENERAL MEETING OF SHAREHOLDERS TO BE HELD ON JUNE 19, 2024 AT 3 DUBLIN LANDINGS, NORTH WALL QUAY, DUBLIN 1, IRELAND

Important Notice Regarding the Availability of Proxy Materials
for the Annual General Meeting of Shareholders
to be held on June 19, 2024
This proxy statement, our 2023 annual report to shareholders
and our Irish Statutory Financial Statements for the year ended December 31, 2023 are available at
https://central.proxyvote.com/pv/web
for viewing, downloading and printing.

A copy of our Annual Report on Form 10-K for the year ended December 31, 2023 as filed with the Securities and Exchange Commission, or SEC, except for exhibits, and our Irish Statutory Financial Statements for the year ended December 31, 2023 will be furnished without charge to any shareholder upon written or oral request to the Company at Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, Ireland, Attention: Secretary, Telephone: +353 1 9038354.

Instead of mailing a printed copy of our proxy materials to all of our shareholders, we provide access to these materials via the Internet. This reduces the amount of paper necessary to produce these materials as well as the costs associated with mailing these materials to all shareholders. Accordingly, on or about April 26, 2024, we will mail a Notice of Internet Availability of Proxy Materials, or Notice, to our shareholders (other than those who previously requested electronic or paper delivery of proxy materials), directing shareholders to a website where they can access our proxy materials, including this proxy statement, our 2023 annual report to shareholders and our Irish Statutory Financial Statements for the year ended December 31, 2023, and view instructions on how to vote via the Internet or by telephone. If you would prefer to receive a paper copy of our proxy materials, please follow the instructions included in the Notice.

INFORMATION ABOUT THE ANNUAL GENERAL MEETING AND VOTING

This proxy statement is furnished in connection with the solicitation of proxies by the board of directors (the "board of directors" or the "board") of Iterum Therapeutics plc (the "Company," "Iterum," "we" or "us") for use at the Annual General Meeting of Shareholders (the "AGM") to be held on June 19, 2024, beginning at 3.00 p.m., Irish time (10.00 a.m., Eastern Time), at 3 Dublin Landings, North Wall Quay, Dublin 1, Ireland and at any adjournment or postponement thereof. On April 24, 2024, the record date for the determination of shareholders entitled to vote at the AGM, there were issued, outstanding and entitled to vote an aggregate of 16,554,885 of our ordinary shares, nominal value $0.01 per share ("ordinary shares"). Each ordinary share entitles the record holder thereof to one vote on each of the matters to be voted on at the AGM.

We have engaged Morrow Sodali LLC ("Morrow Sodali"), to assist with the solicitation of proxies on our behalf. Please contact Morrow Sodali with any queries:

Morrow Sodali LLC
333 Ludlow Street
5th Floor, South Tower
Stamford, CT 06902

Shareholders May Call:
800-662-5200

Banks & Brokers May Call:
203-658-9400

Your vote is important no matter how many shares you own. Please take the time to vote. Take a moment to read the instructions below. Choose the way to vote that is easiest and most convenient for you and cast your vote as soon as possible.

If you are the "record holder" of your shares, meaning that you own your shares in your own name and not through a bank, broker or other nominee, you may vote in one of four ways:

(1) *You may vote over the Internet.* You may vote your shares by following the "Online" instructions on the enclosed proxy card. If you vote over the Internet, you do not need to vote by telephone or complete and mail your proxy card. The internet voting facilities for eligible shareholders of record will close at 4.59 a.m., Irish time on June 19, 2024 (11.59 pm, Eastern Time on June 18, 2024).

(2) *You may vote by telephone.* You may vote your shares by following the "Phone" instructions on the enclosed proxy card. If you vote by telephone, you do not need to vote over the Internet or complete and mail your proxy card. If you vote by telephone, your use of that telephone system, and specifically the entry of your pin number/other unique identifier, will be deemed to constitute your appointment, in writing and under hand, and for all purposes of the Irish Companies Act 2014, of each of David G. Kelly, Louise Barrett and Kevin Dalton as your proxy to vote your shares on your behalf in accordance with your telephone instructions. The telephone voting facilities for eligible shareholders of record will close at 4.59 a.m., Irish time on June 19, 2024 (11.59 pm, Eastern Time on June 18, 2024).

(3) *You may vote by mail.* You can vote by completing, dating and signing the proxy card provided to you and promptly mailing it in the provided postage-paid envelope. If you vote by mail, you do not need to vote over the Internet or by telephone. We must receive the completed proxy card by 5.00 p.m., Irish time (12.00 p.m., Eastern Time), on June 18, 2024.

(4) *You may vote in person.* If you attend the AGM, you may vote by delivering your completed proxy card in person or you may vote by completing a ballot at the AGM. Ballots will be available at the AGM. You may obtain directions to the location of the AGM by requesting them in writing or by telephone as follows: c/o Secretary, Iterum Therapeutics plc, Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, Ireland, Phone: +353 1 9038354.

All proxies that are executed and delivered by mail or in person or are otherwise submitted online or by telephone will be voted on the matters set forth in the accompanying Notice of Annual General Meeting of Shareholders in accordance with the shareholders' instructions. However, if no choice is specified on a proxy as to one or more of the proposals, the proxy will be voted in accordance with the board of directors' recommendations on such proposals as set forth in this proxy statement. All proxies will be forwarded to the Company's registered office electronically.

After you have submitted a proxy, you may still change your vote and revoke your proxy prior to the AGM by doing any one of the following things:

- submitting a new proxy by following the "Online" or "Phone" instructions on the enclosed proxy card at a date later than your previous vote but prior to the voting deadline (which is 4.59 a.m., Irish time on June 19, 2024 (11.59 pm, Eastern Time on June 18, 2024));

- signing another proxy card and either arranging for delivery of that proxy card by mail to the registered office of the Company prior to the start of the AGM, or by delivering that signed proxy card in person at the AGM;
- giving our Secretary a written notice before or at the AGM that you want to revoke your proxy; or
- voting in person at the AGM.

Your attendance at the AGM alone will not revoke your proxy.

If the shares you own are held in "street name" by a bank, broker or other nominee record holder, which we collectively refer to in this proxy statement as "brokerage firms," your brokerage firm, as the record holder of your shares, is required to vote your shares according to your instructions. To vote your shares, you will need to follow the directions your brokerage firm provides you. Many brokerage firms also offer the option of voting over the Internet or by telephone, instructions for which, if available, would be provided by your brokerage firm on the voting instruction form that it delivers to you. Because many brokerage firms are member organizations of the New York Stock Exchange ("NYSE"), the rules of the NYSE will likely govern how your brokerage firm would be permitted to vote your shares in the absence of instruction from you. Under the current rules of the NYSE, if you do not give instructions to your brokerage firm, it may still be able to vote your shares with respect to certain "discretionary" items but will not be allowed to vote your shares with respect to certain "non-discretionary" items. Proposal No. 2 (ratification of KPMG as our independent registered public accounting firm) is expected to be considered a discretionary item under the rules of the NYSE and therefore your brokerage firm may be able to vote on that item even if it does not receive instruction from you, provided it holds your shares in its name. In the event a bank, broker or other nominee record holder determines that it does not have authority or otherwise does not exercise discretionary authority to vote on Proposal No. 2, it may deliver "broker non-votes" for such shares. Proposal No. 1 (election of the Class III directors), Proposal No. 3 (advisory, non-binding, vote on the compensation of our named executive officers) and Proposal No. 4 (advisory, non-binding, vote on the frequency of future votes on the compensation of our named executive officers) are expected to be considered "non-discretionary" items, and therefore if you do not instruct your brokerage firm on how to vote with respect to Proposals 1, 3 or 4, we expect that your brokerage firm will not be able to vote with respect to such proposals and will deliver "broker non-votes" for such shares.

If your shares are held in street name, you must bring an account statement from your brokerage firm showing that you are the beneficial owner of the shares as of the record date (April 24, 2024) to be admitted to the AGM. To be able to vote your shares held in street name at the AGM, you will need to request a "legal proxy" from the bank, broker or nominee.

Votes Required

One or more Members (as defined in the Company's Constitution) whose name is entered in the register of members of the Company as a registered holder of the Company's 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 the issued and outstanding ordinary shares of the Company entitled to vote at the AGM, will constitute a quorum for the transaction of business at the AGM. Ordinary shares represented in person or by proxy (including "broker non-votes" (as described above) and shares which abstain or do not vote with respect to one or more of the matters presented for shareholder approval) will be counted for the purposes of determining whether a quorum is present at the AGM. The following votes are required for approval of the proposals being presented at the AGM:

Proposal No. 1: To elect the Class III directors. The affirmative vote of the holders of ordinary shares representing a majority of the votes cast on the matter and voting affirmatively or negatively is required for the election of a director nominee.

Proposal No. 2: To ratify, in a non-binding vote, the appointment of KPMG to serve as our independent registered public accounting firm for the fiscal year ended December 31, 2024 and to authorize the board of directors, acting through the audit committee, to set the independent registered public accounting firm's remuneration. The affirmative vote of the holders of ordinary shares representing a majority of the votes cast on the matter and voting affirmatively or negatively is required for the ratification of the appointment of KPMG as our independent registered public accounting firm for the current fiscal year and to authorize the board of directors, acting through the audit committee, to set the independent registered public accounting firm's remuneration.

Proposal No. 3: To vote on an advisory, non-binding, resolution to approve the compensation of our named executive officers. This proposal calls for an advisory, non-binding, vote, and accordingly there is no "required vote" that would constitute approval. Our board, including our compensation committee, values the opinions of our shareholders and, to the extent there are a substantial number of votes cast against the executive compensation as disclosed in this proxy statement, we will consider our shareholders' concerns and evaluate what actions may be appropriate to address those concerns.

Proposal No. 4: To vote on an advisory, non-binding, proposal on the frequency of future advisory votes on the compensation of our named executive officers. This proposal provides a choice among three frequency periods (every one, two or three years) for future advisory votes on named executive officer compensation. With respect to this proposal, if none of the frequency periods receives a simple majority of the votes cast, the frequency period that has received the

most votes will be deemed to be the recommendation of our shareholders. However, because this vote is advisory and not binding on our board (or any committee thereof), we may decide that it is in the best interests of us and our shareholders to hold a vote regarding the compensation of our named executive officers more or less frequently than the frequency period recommended by our shareholders.

Shares that abstain from voting as to a particular matter and any broker non-votes will not be counted as votes in favor of such matter and will also not be counted as shares voting on such matter. Accordingly, abstentions and broker non-votes will have no effect on the voting on the proposal referenced above.

SHARE OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of March 31, 2024 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 Securities and Exchange Commission (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 March 31, 2024, restricted share units that vest within 60 days of March 31, 2024, shares issuable upon exercise of warrants within 60 days of March 31, 2024, and shares issuable upon exchange of our outstanding 6.500% exchangeable senior subordinated notes due 2025 (the "Exchangeable Notes") (assuming physical settlement), which are exchangeable within 60 days of March 31, 2024. Our ordinary shares issuable pursuant to share options, restricted share units, warrants and Exchangeable Notes, but not taking into account any additional ordinary shares issuable to satisfy accrued and unpaid interest due upon exchange of any Exchangeable Notes, are deemed outstanding for computing the percentage of the person holding such share options, restricted share units, warrants or Exchangeable Notes 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 16,470,414 ordinary shares outstanding on March 31, 2024. Except as otherwise set forth below, the address of the beneficial owner is c/o Iterum Therapeutics plc, Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, Ireland.

	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% Shareholders:		
Entities affiliated with Point72 Asset Management, L.P.[(1)]	850,001	5.2%
Directors and Named Executive Officers:		
Corey N. Fishman[(2)]	158,023	*
Sailaja Puttagunta[(3)]	109,928	*
Judith M. Matthews[(4)]	45,006	*
Michael Dunne, MD[(5)]	116,831	*
Beth P. Hecht	18,839	*
Ronald M. Hunt[(6)]	468,603	2.8%
David G. Kelly[(7)]	54,323	*
All current executive officers and directors as a group (7 persons)[(7)])	971,553	5.6%

* less than 1%

(1) This information is based solely upon information set forth on Schedule 13G filed jointly by Point72 Asset Management, L.P. ("Point72 Asset Management"), Point72 Capital Advisors, Inc. ("Point72 Capital Advisors Inc."), Cubist Systematic Strategies, LLC ("Cubist Systematic Strategies"), and Steven A. Cohen ("Mr. Cohen") with the SEC on January 30, 2024. Consists of (i) 850,000 shares reported as beneficially owned by Point72 Asset Management, Point72 Capital Advisors Inc. and Mr. Cohen; and (ii) 1 share reported as beneficially owned by Cubist Systematic Strategies and Mr. Cohen. Point72 Asset Management and Point72 Capital Advisors Inc. each reported sole voting power with respect to zero shares, shared voting power with respect to 850,000 shares, sole dispositive power with respect to zero shares and shared dispositive power with respect to 850,000 shares. Cubist Systematic Strategies reported sole voting power with respect to zero shares, shared voting power with respect to 1 share, sole dispositive power with respect to zero shares and shared dispositive power with respect to 1 share. Mr Cohen reported sole voting power with respect to zero shares, shared voting power with respect to 850,001 shares, sole dispositive power with respect to zero shares and shared dispositive power with respect to 850,001 shares. Point72 Asset Management, Point72 Capital Advisors Inc., Cubist Systematic Strategies, and Mr. Cohen own no shares directly. Pursuant to an investment management agreement, Point72 Asset Management maintains investment and voting power with respect to the securities held by Point72 Associates, LLC. Point72 Capital Advisors Inc. is the general partner of Point72 Asset Management. Pursuant to an investment management agreement, Cubist Systematic Strategies maintains investment and voting power with respect to the securities held by an investment fund it manages. Mr. Cohen controls each of Point72 Asset Management, Point72 Capital Advisors Inc., and Cubist Systematic Strategies. The address of the principal business office of (i) Point72 Asset Management, Point72 Capital Advisors Inc., and Mr. Cohen, is 72 Cummings Point Road, Stamford, CT 06902; and (ii) Cubist Systematic Strategies, is 55 Hudson Yards, New York, NY 10001.

(2) Consists of (a) 54,449 shares beneficially owned by Mr. Fishman, and (b) 103,574 shares issuable to Mr. Fishman pursuant to share options exercisable within 60 days of March 31, 2024.

(3) Consists of (a) 10,369 shares beneficially owned by Dr. Puttagunta, and (b) 99,559 shares issuable to Dr. Puttagunta pursuant to share options exercisable within 60 days of March 31, 2024.

(4) Consists of (a) 8,135 shares beneficially owned by Ms. Matthews, and (b) 36,871 shares issuable to Ms. Matthews pursuant to share options exercisable within 60 days of March 31, 2024.

(5) Consists of (a) 113,754 shares beneficially owned by Dr. Dunne, and (b) 3,077 shares issuable to Dr. Dunne pursuant to warrants exercisable within 60 days of March 31, 2024.

(6) 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 March 31, 2024; and (c) (i) 71,445 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 71,445 shares, shared voting power with respect to zero shares, sole dispositive power with respect to 71,445 shares and shared dispositive power with respect to zero shares, (ii) 25,641 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 25,641 shares, shared voting power with respect to zero shares, sole dispositive power with respect to 25,641 shares and shared dispositive power with respect to zero shares, and (iii) 230,578 shares issuable to NLV-III and 82,707 shares issuable to NBPO-II on exchange of the Exchangeable Notes held by them and exchangeable within 60 days of March 31, 2024 (assuming physical settlement). 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.

(7) 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 March 31, 2024.

(8) Includes (a) 319,451 shares held by the current directors and executive officers and their affiliates, (b) 335,740 shares issuable to the current directors and executive officers pursuant to share options exercisable within 60 days of March 31, 2024, (c) 3,077 shares issuable to the current directors pursuant to warrants exercisable within 60 days of March 31, 2024, and (d) 313,285 shares issuable to affiliates of current directors on exchange of the Exchangeable Notes within 60 days of March 31, 2024 (assuming physical settlement).

MANAGEMENT AND CORPORATE GOVERNANCE MATTERS

Board of Directors

Our business and affairs are managed under the direction of our board of directors. Our Articles of Association (the "Articles of Association") provide that the number of directors shall not be less than two (2) nor more than thirteen (13), with the exact number to be determined by the board. Our board currently consists of five (5) members divided among three classes with staggered three-year terms as follows:

(1) Class I, whose sole member is David G. Kelly. The term of the Class I director will expire at our 2025 annual general meeting of shareholders;

(2) Class II, whose members are Beth P. Hecht and Michael Dunne. The terms of the Class II directors will expire at our 2026 annual general meeting of shareholders; and

(3) Class III, whose members are Corey N. Fishman and Ronald M. Hunt. The terms of the Class III directors will expire at the AGM.

In April 2024, our board of directors accepted the recommendation of the nominating and corporate governance committee and voted to nominate Mr. Fishman and Mr. Hunt for election at the AGM for a term of three years to serve until the 2027 annual general meeting of shareholders subject to their earlier death, resignation, retirement, disqualification or removal.

Continuing Members of and Current Members who are Nominated for Election to our Board of Directors

Set forth below are the names of each continuing member of, and the current members who are nominated for election to, our board of directors, their ages, their principal occupation and business experience for at least the past five years and the names of other public companies of which each director has served as a director during the past five years, in each case as of March 31, 2024. Additionally, set forth below is information about the specific experiences, qualifications, attributes or skills that led our board of directors to the conclusion on suitability of each person to serve as a director.

Name	Age	Position
Corey N. Fishman	59	Director, President and Chief Executive Officer
Michael W. Dunne	64	Director
Beth P. Hecht [(1)(2)]	60	Director
Ronald M. Hunt [(1)(2)(3)]	59	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, 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. Since December 2020 Dr. Dunne has 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 and served as a consultant for us until March 31, 2022 and has served as a consultant for one of our wholly-owned subsidiaries since December 2020. From November 2014 until September 2015, Dr. Dunne was vice president of research and development at Actavis plc. 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.

Former Members of our Board of Directors

Brenton K. Ahrens served as a member of our board of directors from November 2015 to May 2023, and as a member of our audit committee from February 2016 to May 2023 and nominating and corporate governance committee from March 2021 to May 2023.

Mark Chin served as a member of our board of directors from May 2017 to December 2023, as a member of our compensation committee from September 2017 to December 2023 and as a member of our audit committee from May 2018 to December 2023.

Composition of the Board of Directors and Meetings

As outlined above, our Articles of Association provide that the number of directors shall not be less than two (2) nor more than thirteen (13), with the exact number to be determined by the board, currently five (5).

Under the Irish Companies Act 2014, and notwithstanding anything contained in our Articles of Association or in any agreement between us and any director, our shareholders may, by an ordinary resolution, remove a director from office before the expiration of his or her term, at a meeting held on no less than 28 days' notice and at which the director is entitled to be heard. Our Articles of Association also provide that the office of a director will be vacated in certain circumstances including if the director resigns his or her office by notice in writing or is requested to resign in writing by not less than a majority of the other directors. 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. If the board fills a vacancy, the director will hold this position as a director for a term that will coincide with the remaining term of the relevant class of director.

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 Securities Exchange Act of 1934, as amended (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".

Nasdaq Diversity Matrix

In accordance with Nasdaq's Board Diversity Rule, we have included our board diversity matrix in this proxy statement as set forth below.

Board Diversity Matrix (as of April 26, 2024)

Total Number of Directors			**5**	
Part I: Gender Identity	**Female**	**Male**	**Non-Binary**	**Did Not Disclose Gender**
Directors	1	4	0	0
Part II: Demographic Background				
African American or Black	0	0		
Alaskan Native or Native American	0	0		
Asian	0	0		
Hispanic or Latinx	0	0		
Native Hawaiian or Pacific Islander	0	0		
White	1	4		
Two or More Races or Ethnicities	0	0		
LGBTQ+	0	0		
Did Not Disclose Orientation	0	0		

Our board diversity matrix as of March 16, 2023 can be found in the proxy statement for our 2023 Annual General Meeting of Shareholders, which was filed with the SEC on March 16, 2023.

Meetings of the Board of Directors

Our board holds at least four regular meetings each year. Directors are expected to attend all meetings of the board and any committees on which they serve.

Our Articles of Association provide that each director and the auditors are entitled to attend and speak at any general meetings of shareholders of the Company. All of our directors attended our annual general meeting of shareholders in 2023.

Our board of directors met 8 times during 2023 and acted by written consent 5 times. During 2023, no incumbent directors attended less than 75% of the aggregate of (i) the total number of meetings of the board and (ii) the total number of meetings of committees of the board on which he/she served, if any.

Board Leadership Structure

Ronald M. Hunt, an independent director under applicable Nasdaq rules, currently serves as chairman of our board. Mr. Hunt's duties as chairman of the board include determining the frequency and length of board meetings, recommending when special meetings of the board should be held, preparing or approving the agenda for each board meeting, chairing meetings of the board and of our independent directors, meeting with any director who is not adequately performing his or her duties as a member of the board or any committee of the board, facilitating communications between management and the board of directors, and assisting with other corporate governance matters.

Our board of directors believes that separating the duties of the chairman of the board from the duties of our chief executive officer enhances the board's oversight of, and independence from, management, while also allowing our chief executive officer to focus on our day-to-day business operations instead of board administration.

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, which was established in accordance with Section 3(a)(58)(A) of the Exchange Act, consists of David G. Kelly, Ronald M. Hunt and Beth P. Hecht. The chairperson of our audit committee is Mr. Kelly. The primary purpose of the audit committee is to discharge the responsibilities of our board of directors with respect to our accounting, financial, and other reporting and internal control practices and to oversee our independent registered public accounting firm. Specific responsibilities of our audit committee include:

- recommending a qualified firm to serve as the independent registered public accounting firm to audit our financial statements to the board of directors;
- helping to ensure the independence and performance of the independent registered public accounting firm;
- discussing the scope and results of the audit with the independent registered public accounting firm, and reviewing, with management and the independent accountants, our interim and year-end operating results;
- reviewing, upon completion of the audit, the Irish Statutory Financial Statements proposed to be filed with our annual return at the Irish Companies Registration Office;
- developing procedures for employees to submit concerns anonymously about questionable accounting or audit matters;
- reviewing related party transactions;
- coordinating the board of directors' oversight of our internal controls over financial reporting, including discussing with management and the independent registered public accounting firm the integrity of our financial reporting processes and internal controls;
- overseeing cybersecurity risk management and providing regular reports to the board of directors addressing cybersecurity as part of our overall risk management program;
- reviewing updates from management and providing feedback regarding cybersecurity matters, including cybersecurity risks and/or incidents and related responses on our cybersecurity position;
- approving (or, as permitted, pre-approving) all audit and all permissible non-audit services to be performed by the independent registered public accounting firm;
- discussing the Company's policies with respect to risk assessment and risk management, including guidelines and policies to govern the process by which the Company's exposure to risk is handled; and
- supporting the board in minimizing the risks related to invested capital and ensuring that management administers the Company's investment portfolio in accordance with the guidelines set out in the corporate investment policy.

Our board of directors has determined that Messrs. Kelly and Hunt and Ms. Hecht each satisfy the independence standards for such committee established by the SEC and the Nasdaq Stock Market.

Our board of directors has determined that Mr. Kelly is an "audit committee financial expert" within the meaning of SEC regulations. Our board of directors has also determined that each member of our audit committee has the requisite financial expertise required under the applicable requirements of the Nasdaq Stock Market. In arriving at this determination, the board of directors has examined each audit committee member's scope of experience and the nature of their employment in the corporate finance sector.

Our audit committee met 4 times in 2023 and acted by written consent 2 times in 2023.

Compensation Committee

Our compensation committee consists of Ronald M. Hunt and Beth P. Hecht. The chairperson of our compensation committee is Mr. Hunt.

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

- reviewing and approving, or recommending that our board of directors approve, the compensation of our executive officers;
- reviewing and recommending to our board of directors the compensation of our directors;
- administering our share and equity incentive plans and delegating authority to subcommittees of the compensation committee to grant share awards under our equity incentive plans to persons who are then subject to Section 16 of the Exchange Act;
- selecting independent compensation consultants, legal counsel or other advisors;
- interpreting and implementing our Compensation Recovery Policy ("Clawback Policy") in a manner that is consistent with NASDAQ Listing Rule 5608 and any other applicable law, and, if practicable and necessary, determining the appropriate means to recover erroneously awarded incentive-based compensation;
- reviewing and approving, or recommending that our board of directors approve, incentive compensation and equity plans, severance agreements, change-of-control protections and any other compensatory arrangements for our executive officers; and
- reviewing and making recommendations to our board of directors regarding incentive compensation and equity plans.

Our compensation committee met 2 times in 2023 and acted by written consent 2 times in 2023.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Ronald M. Hunt and David G. Kelly. The chairperson of our nominating and corporate governance committee is Mr. Hunt.

Specific responsibilities of our nominating and corporate governance committee include:

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

Our nominating and corporate governance committee met 2 times in 2023 and acted by written consent 1 time in 2023.

Board Processes

Oversight of Risk

Our board of directors oversees our risk management processes directly and through its committees. Our management is responsible for risk management on a day-to-day basis. The role of our board and its committees is to oversee the risk management activities of management. They fulfill this duty by discussing with management the policies

and practices utilized by management in assessing and managing risks and providing input on those policies and practices. In general, our board oversees risk management activities relating to business strategy, acquisitions, capital raising and allocation, organizational structure and certain operations risks; our audit committee oversees risk management activities related to financial risk exposures and the steps management has taken to monitor and control these exposures, as well as legal and compliance risks and risks relating to cybersecurity; our nominating and corporate governance committee oversees risk management activities relating to board composition and management succession planning and monitors the effectiveness of our corporate governance guidelines; and our compensation committee oversees risk management activities relating to our compensation policies and practices. Each committee reports to the full board on a regular basis, including reports with respect to the committee's risk oversight activities as appropriate. In addition, since risk issues often overlap, committees from time to time request that the full board discuss such risks.

Director Nomination Process

Generally, the board will be responsible for nominating directors for election to the board by the Company's shareholders at the annual general meeting of shareholders and the persons to be elected by the board to fill any vacancies on the board. The nominating and corporate governance committee is responsible for identifying, reviewing and evaluating and recommending to the board candidates to serve as directors of the Company, in accordance with its charter and consistent with the criteria set by the board in our corporate governance guidelines described below under "Corporate Governance Guidelines". The board believes that candidates for director should have certain minimum qualifications, including being able to read and understand basic financial statements, being over 21 years of age and having the highest personal integrity and ethics. In making such recommendations, the nominating and corporate governance committee shall consider candidates proposed by the Company's shareholders and shall review and evaluate information available to it regarding such candidates and shall apply the same criteria and shall follow substantially the same process in considering them, as it does in considering other candidates. Shareholders may nominate individuals as potential director candidates by submitting their names, together with appropriate biographical information and background materials, and information with respect to the shareholder or group of shareholders making the nomination, including the number of ordinary shares owned by such shareholder or group of shareholders, in writing to the nominating and corporate governance committee, c/o Secretary, Iterum Therapeutics plc, Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, Ireland. The nominating and corporate governance committee will evaluate shareholder-recommended candidates by following substantially the same process outlined above.

The nominating and corporate governance committee shall also administer the process outlined in our Articles of Association concerning shareholder nominations for director candidates. Shareholders must follow the formal procedures described in our Articles of Association and in "Shareholder Proposals for 2024 Annual General Meeting of Shareholders" below in connection with any such nomination.

The nominating and corporate governance committee has not adopted a formal diversity policy but will consider issues of diversity among its members in identifying and considering nominees for director as well as age, skill and such other factors as it deems appropriate given the current needs of the board and the Company, to maintain a balance of knowledge, experience and capability.

Corporate Governance Guidelines

Our board of directors has adopted corporate governance guidelines to assist in the exercise of its duties and responsibilities and to serve the best interests of our Company and shareholders. The guidelines provide that:

- the core responsibility of our board is to provide oversight of, and strategic guidance to, senior management;
- the board will be composed of not less than a majority of independent directors, subject to any exceptions permitted by Nasdaq listing standards;
- the independent directors of the board will meet periodically in executive session at least two times per year or such greater number as required by the Nasdaq listing standards;
- board members have complete and open access to our management; and
- the nominating and corporate governance committee will conduct an annual self-evaluation to determine whether the board and its committees are functioning effectively.

A copy of the Corporate Governance Guidelines is publicly available on our website at https://www.iterumtx.com/.

Shareholder Communications to the Board of Directors

Shareholders who have questions or concerns should contact our Investor Relations department at +1 312 778 6073 or by email to IR@iterumtx.com. Shareholders who wish to address questions regarding our business directly with the board of directors, or any individual director, should direct his or her questions in writing to Board of Directors c/o Secretary, Iterum Therapeutics plc, Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, Ireland. Communications will be distributed to the board of directors, or to any individual director or directors as appropriate, depending on the facts and circumstances outlined in the communications. Communications will be forwarded to other directors if they relate to substantive matters that the chairman of our board, in consultation with legal counsel, considers appropriate for attention by the other directors. In general, communications relating to corporate governance and long-term corporate

strategy are more likely to be forwarded than communications relating to ordinary business affairs, personal grievances or matters as to which we receive repetitive or duplicative communications.

Compensation Committee Interlocks and Insider Participation

During 2023, the members of our compensation committee were Ronald M. Hunt (Chairman), Mark Chin and Beth P. Hecht. No member of our compensation committee is, or has ever been, an officer or employee of our Company. None of our executive officers serve, or have served during the last year, as a member of the board of directors, compensation committee, or other board committee performing equivalent functions of any other entity that has one or more executive officers serving as one of our directors or on our compensation committee.

Executive Officers

The following table sets forth information regarding our executive officers as of March 31, 2024:

Name	Age	Position
Corey N. Fishman	59	Director, President and Chief Executive Officer
Sailaja Puttagunta	55	Chief Medical Officer
Judith M. Matthews	54	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 Dr. Puttagunta and Ms. Matthews:

Dr. Sailaja Puttagunta has served as our Chief Medical Officer since December 2021, and previously served as our Vice President of Clinical Development from January 2016 to December 2018. From October 2019 to December 2021, Dr. Puttagunta served as chief medical officer at BiomX Inc., a public biotechnology company, and from December 2018 to October 2019, she served as chief medical officer of BiomX Ltd. until its merger with BiomX, Inc. in October 2019. From January 2015 to January 2016, Dr. Puttagunta served as vice president of medical affairs at Allergan plc, formerly Actavis plc, a pharmaceutical company. From August 2014 to December 2014, Dr. Puttagunta served as vice president of development and medical affairs at Durata Therapeutics, Inc., a pharmaceutical company, and from June 2012 to July 2014, she served as Durata's executive director of clinical and medical affairs. From 2006 to May 2012, Dr. Puttagunta served as a medical director at Pfizer Inc., a pharmaceutical company. Dr. Puttagunta graduated from Gandhi Medical College in Hyderabad, India and completed her residency in Internal Medicine and a fellowship in Infectious Diseases at Yale University School of Medicine. She also holds an M.S. in Biochemistry from the New York University School of Medicine.

Judith M. Matthews has served as our Chief Financial Officer since November 2015. From 2012 to February 2015, Ms. Matthews served as vice president of finance at Durata Therapeutics, Inc. From 2009 to 2012, Ms. Matthews served as head of financial planning & analysis at Bally Total Fitness Corporation, a fitness club chain. From 2004 to 2008, Ms. Matthews served as vice president of finance for the Sterno Group, a subsidiary of Blyth, Inc., a home products company. Ms. Matthews holds a B.A. in accounting from the University of Illinois at Urbana-Champaign and a Master of Management in finance and marketing from the Kellogg School of Management at Northwestern University.

EXECUTIVE OFFICER AND DIRECTOR 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, 2023 and 2022 and to the members of our board of directors for services provided for the year ended December 31, 2023.

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, our Company has retained the services of Coda Advisors LLC, or 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, the compensation committee ultimately makes its own decisions with regard to our executive and director compensation programs.

For the year ended December 31, 2023, the compensation committee reviewed information regarding the independence and potential conflicts of interest of Coda, taking into account, among other things (i) the provision of other services to the Company by Coda; (ii) the amount of fees received by Coda from the Company as a percentage of its total revenue; (iii) Coda's policies and procedures to prevent conflicts of interest; (iv) any business or personal relationships that Coda has with any member of the compensation committee; (v) any shares held by Coda in the Company; and (vi) any business or personal relationship Coda or Coda employees have with any executive officers of the Company. Based on this review, the compensation committee concluded that the engagement did not raise any conflict of interest.

Executive Officer Summary Compensation Table

The following table provides details of the compensation and other benefits paid or accrued by us and our subsidiaries to our named executive officers for the year ended December 31, 2023, who are our President and Chief Executive Officer, Corey N. Fishman, and our two next most highly compensated executive officers, Dr. Sailaja Puttagunta, our 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] ($)	All Other Compensation[4] ($)	Total ($)
Corey N. Fishman	2023	611,831	360,311	—	220,000	320,709	5,960	1,518,811
President and Chief Executive Officer	2022	588,758	486,906	—	—	292,144	4,902	1,372,710
Sailaja Puttagunta	2023	492,417	237,263	—	60,000	211,185	5,960	1,006,825
Chief Medical Officer	2022	475,000	86,000	—	—	192,375	2,519	755,894
Judith M. Matthews	2023	411,211	176,120	—	80,000	156,763	3,680	827,774
Chief Financial Officer	2022	395,395	238,000	—	—	142,800	2,622	778,817

(1) The amounts reported in the "Bonus" column for Mr. Fishman and Ms. Matthews during 2023 and 2022 and the amounts paid to Dr. Puttagunta during 2023 reflect certain discretionary cash bonuses paid to our executive officers to incentivize the continued dedication of executives and the amount reported in the "Bonus" column for Dr. Puttagunta during 2022 reflects a bonus paid to Dr. Puttagunta within 30 days of the six month anniversary of her commencing employment in accordance with the terms of her offer letter with Iterum Therapeutics US Limited.
(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, or FASB, Accounting Standards Codification, or ASC, 718. Assumptions used in the calculation of these amounts are included in Note 13 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, 2023 and 2022, respectively. Amounts disclosed for the year ended December 31, 2023 exclude payments made in 2023 for 2022 bonuses. Amounts disclosed for the year ended December 31, 2022 exclude payments made in 2022 for 2021 bonuses.
(4) Includes the dollar value of life insurance premiums paid by the company for the benefit of such executive.

Narrative Disclosure to Executive Officer Summary Compensation Table

Base Salary

During the year ended December 31, 2023, we paid annualized base salaries of $613,798 to Mr. Fishman, $494,000 to Dr. Puttagunta and $412,533 to Ms. Matthews. During the year ended December 31, 2022, we paid annualized base salaries of $590,190 to Mr. Fishman, $475,000 to Dr. Puttagunta and $396,666 to Ms. Matthews.

In February 2024, our compensation committee approved an increase to the annualized base salaries of our executive officers, effective February 1, 2024, as follows: $632,212 for Mr. Fishman, $516,230 for Dr. Puttagunta and $431,097 for Ms. Matthews.

None of the named executive officers are currently party to any employment arrangements that provide for automatic or scheduled increases in base salary.

Non-Equity Incentive Plan Compensation

Our named executive officers participate in a cash bonus program which is tied to the achievement of strategic and corporate goals of the Company, which are approved annually by our compensation committee. Our compensation committee determines the amount of these bonuses, if any, based on its assessment of the named executive officers' performance and that of the Company against goals established annually.

Under their respective employment agreements, the annual target bonus for Mr. Fishman is 55% of his current base salary, the annual target bonus for Dr. Puttagunta is 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, the 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. The compensation committee recommended cash bonus payments of $292,144 to Mr. Fishman, $192,375 to Dr. Puttagunta and $142,800 to Ms. Matthews with respect to the year ended December 31, 2022.

Bonuses

During 2022, the compensation committee also recommended special retention bonus payments for executives of $486,906 to Mr. Fishman and $238,000 to Ms. Matthews on the achievement of certain milestones to incentivize the continued dedication of executives. In connection with her commencement of employment and pursuant to the terms of her employment agreement, Dr. Puttagunta was paid $86,000 within thirty days of the six month anniversary of her start date.

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 on the achievement of certain milestones to incentivize the continued dedication of executives.

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.

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.

No equity-based awards were granted to executives in 2022. On July 7, 2022, we entered into share option cancellation agreements with each of Mr. Fishman and Ms. Matthews pursuant to which Mr. Fishman and Ms. Matthews agreed to the surrender and cancellation of certain previously granted share options to purchase ordinary shares in order to make available additional shares under our 2018 Plan. The aggregate number of shares underlying the options surrendered by each such officer was as follows: Mr. Fishman, 8,487 ordinary shares, at an exercise price of $195 per share, 10,000 ordinary shares, at an exercise price of $87 per share and 352,000 ordinary shares, at an exercise price of $30.15 per share; Ms. Matthews, 1,591 ordinary shares, at an exercise price of $195 per share, 2,000 ordinary shares, at an exercise price of $87 per share and 129,066 ordinary shares, at an exercise price of $30.15 per share.

Outstanding Equity Awards at December 31, 2023

The following table presents information regarding outstanding equity awards held by our named executive officers as of December 31, 2023. All equity awards were granted under our 2015 Equity Incentive Plan, our 2018 Plan and our 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	—	—
	—	275,000 [4]	$ 1.00	03/31/2031	—	—
Sailaja Puttagunta	60,000 [5]	60,000 [5]	$ 7.27	9/12/2031	—	—
	—	75,000 [4]	$ 1.00	03/31/2031	—	—
	—	—	—	—	16,666 [6]	$ 32,832
Judith M. Matthews	792 [3]	—	$ 49.50	09/11/2027	—	—
	—	100,000 [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.
(5) Share option that vested as to 25% of the ordinary shares underlying the share option on December 1, 2022 with the remaining ordinary shares vesting in equal monthly installments thereafter until December 1, 2025, subject to continued service with us through each relevant vesting date. This award was granted under our 2021 Inducement Plan as an inducement material to Dr. Puttagunta's acceptance of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).
(6) Restricted share units that vested as to 25% of the shares underlying the award on December 1, 2022 with the remaining shares scheduled to vest annually in three equal installments thereafter, subject to continued service with us through each relevant vesting date. This award was granted under our 2021 Inducement Incentive Plan as an inducement material to Dr. Puttagunta's acceptance of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).

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.

Sailaja Puttagunta serves as our Chief Medical Officer. On October 27, 2021, Dr. Puttagunta entered into an offer letter with Iterum Therapeutics US Limited, our indirect wholly owned subsidiary. The offer letter has no specific term and constitutes an at-will employment arrangement. Dr. Puttagunta commenced employment on December 1, 2021. Dr. Puttagunta's base salary is $475,000 and her discretionary annual target performance bonus is 45% of her annual base salary. Dr. Puttagunta was also entitled to an initial bonus payment of $86,000 within 30 days of commencing employment and a subsequent bonus payment of $86,000 within 30 days of the six-month anniversary of commencement of employment, conditioned upon Dr. Puttagunta's continuing employment with the Company on such payment date. Dr. Puttagunta's base salary was reviewed in January 2023 and increased to $494,000, effective February 1, 2023. Her base salary was reviewed in January 2024 and increased to $516,230, 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's base salary (twelve months in the case of Mr. Fishman and nine months in the case of Dr. Puttagunta and 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'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's then current base salary in the case of Dr. Puttagunta and Ms. Matthews, and to 18 months of his then current base salary in the case of Mr. Fishman. The executives will also be entitled to an additional cash payment equal to a percentage of such executives' target annual bonus for the year of termination, equal to 100% in the case of Dr. 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, whichever results in the executive receiving the greater amount after taking into consideration the payment of all taxes, including the excise tax under Section 4999 of the Code, in each case based upon the highest marginal rate for the applicable tax.

Payment of any of the severance benefits described above is also conditioned on the named executive officer's delivery and non-revocation of a general release of claims in our favor.

In addition, pursuant to 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, Ms. Matthews and Dr. Puttagunta 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's entitlement to participate are to be determined at the time of the change of control transaction.

Pay Versus Performance

As required by Item 402(v) of Regulation S-K, we are providing the following information about the relationship between "compensation actually paid" to our principal executive officer ("PEO") and the average of our other Named Executive Officers ("NEOs") and certain financial metrics of the Company. The following table also provides information regarding company performance over the same periods as well as the relationship of "compensation actually paid" to our PEO and NEOs to company performance.

Year	Summary Compensation Table Total for PEO ($) [1]	Compensation Actually Paid to PEO ($) [2] [3]	Average Summary Compensation Table Total for non PEO NEOs ($) [4]	Average Compensation Actually Paid to non PEO NEOs ($) [5]	Value of Initial Fixed $100 Investment Based On: Total Shareholder Return ($) [6]	Net Loss ($ in thousands) [7]
2023	1,518,811	1,748,073	917,300	1,011,521	14.29	(38,371)
2022	1,372,710	1,453,333	767,356	732,197	33.50	(44,434)

(1) Reflects compensation (as reported in the Summary Compensation Table) for our PEO, Mr. Corey Fishman, in 2022 and 2023.

(2) Calculated in accordance with Item 402(v)(2) of Regulation S-K. The Compensation Actually Paid Schedule shown below sets forth the adjustments made during each year represented in the Pay Versus Performance Table to arrive at the "compensation actually paid" to our Chief Executive Officer.

Year	Summary Compensation Table Total for PEO ($) [1]	Deductions for Reported Grant Date Fair Value of Stock Awards ($) (a)	Deductions for Reported Grant Date Fair Value of Option Awards (a)	Additions for Pay Versus Performance Equity Adjustments (b)	Compensation Actually Paid ($)
2023	1,518,811	-	(220,000)	449,262	1,748,073
2022	1,372,710	-	-	80,623	1,453,333

a) Reflects the amounts reported in the Stock Awards and Option Awards columns of the Summary Compensation Table in the relevant years.

b) The pay versus performance equity adjustments reflect the aggregated sum of the following values for the respective years:

Year	Year-End Fair Value of Outstanding and Unvested Equity Awards Granted in the Covered Year ($)	Year Over Year Change in Fair Value of Outstanding and Unvested Equity Awards Granted in Prior Years ($)	Year Over Year Change in Fair Value of Equity Awards Granted in Prior Years That Vested in the Covered Year ($)	Total Pay Versus Performance Equity Adjustments ($)
2023	435,502	-	13,760	449,262
2022	-	-	80,623	80,623

(3) Measurement date equity fair values are calculated with assumptions derived on a basis consistent with those used for grant date fair value purposes. RSUs are valued based on the closing stock price on the applicable vesting date(s). Stock options are valued using a Black-Scholes model as at the relevant measurement dates.

(4) Reflects compensation our non-PEO NEOs, Dr. Sailaja Puttagunta and Ms. Judith M. Matthews, in 2022 and 2023. The dollar amounts reported in column (d) represent the average of the compensation reported for the non-PEO NEOs for each corresponding year in the "Total" column of the Summary Compensation Table.

(5) Average "compensation actually paid" for the non-PEO NEOs has been calculated in accordance with Item 402(v)(2) of Regulation S-K. The Compensation Actually Paid Schedule shown below sets forth the adjustments made during each year represented in the Pay Versus Performance Table to arrive at the average "compensation actually paid" to our non-PEO NEOs.

Year	Summary Compensation Table Total ($)	Deductions for Reported Grant Date Fair Value of Stock Awards ($) (a)	Deductions for Reported Grant Date Fair Value of Option Awards ($) (a)	Additions for Pay Versus Performance Equity Adjustments ($) (b)	Compensation Actually Paid ($)
2023	917,300	-	(70,000)	164,221	1,011,521
2022	767,356	-	-	(35,159)	732,197

a) Reflects the average amounts reported in the Stock Awards and Option Awards columns of the Summary Compensation Table in the relevant years.

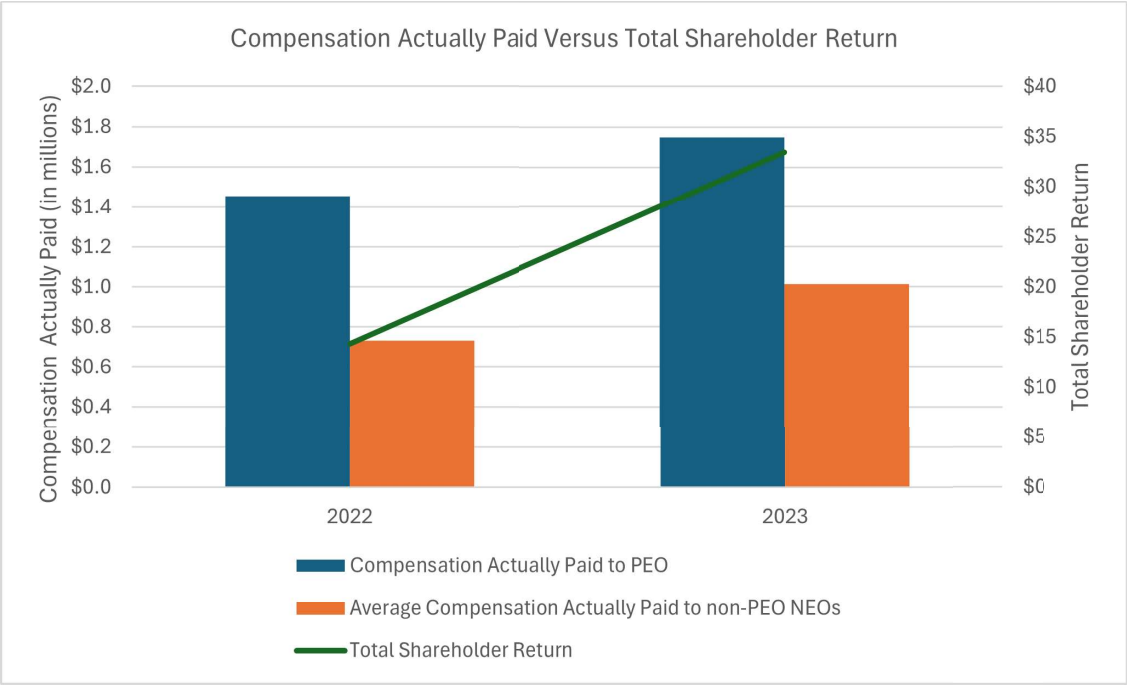
b) The pay versus performance equity adjustments reflect the aggregated sum of the following values for the respective years:

Year	Year-End Fair Value of Outstanding and Unvested Equity Awards Granted in the Covered Year ($)	Year Over Year Change in Fair Value of Outstanding and Unvested Equity Awards Granted in Prior Years ($)	Year Over Year Change in Fair Value of Equity Awards Granted in Prior Years That Vested in the Covered Year ($)	Total Pay Versus Performance Equity Adjustments ($)
2023	138,569	-	25,652	164,221
2022	-	-	(35,159)	(35,159)

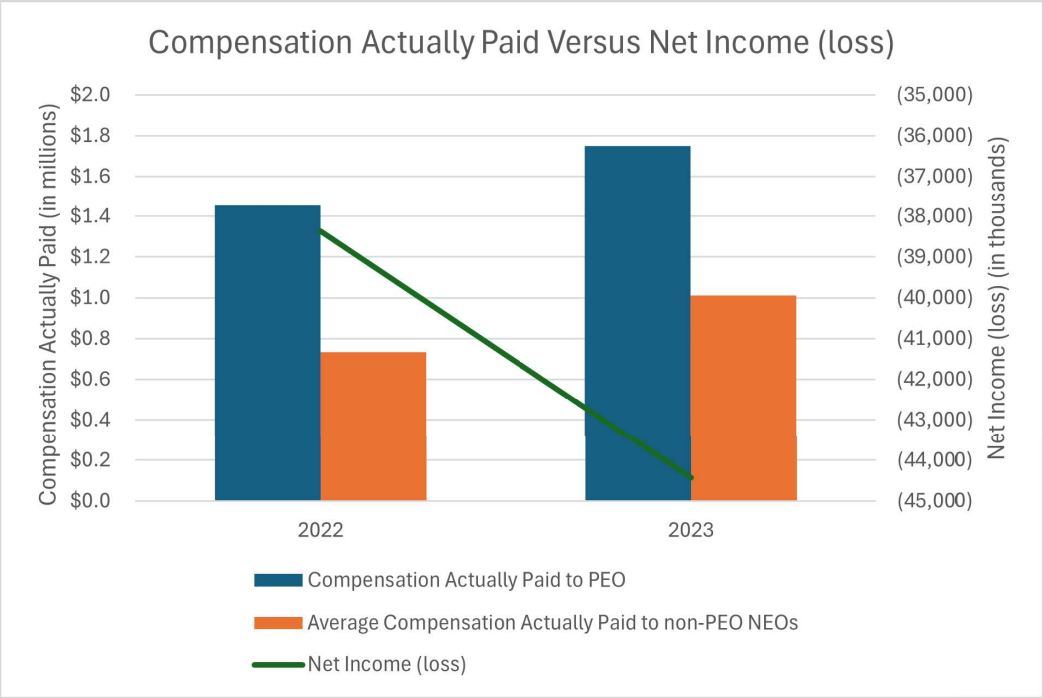
(6) The cumulative total shareholder return amounts reported are calculated by dividing the difference between the Company's share price at the end of the applicable measurement period and the beginning of the measurement period by the Company's share price at the beginning of the measurement period. The Company did not pay any dividends during the measurement periods.

(7) The dollar amounts are the Company's net loss amounts reflected in the Company's audited financial statements for the applicable year.

The following graph visually describes the relationship between "compensation actually paid" to our PEO and the average "compensation actually paid" to our other non-PEO NEOs, to the cumulative total shareholder return of the Company.



The following graph visually describes the relationship between "compensation actually paid" to our PEO and the average "compensation actually paid" to our other non-PEO NEOs, to net income (loss).



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, 2023, 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 ($)	Option Awards [1][2] ($)	Share Awards [1][3] ($)	All Other Compensation [4] ($)	Total ($)
Brenton K. Ahrens [5]	—	—	—	—	—
Mark Chin [6]	68,500	—	—	—	68,500
Michael Dunne, M.D.	55,000		—	60,000	115,000
Beth P. Hecht	68,500		—	—	68,500
Ronald M. Hunt	88,750		—	—	88,750
David G. Kelly	74,000	—	—	—	74,000

(1) The amounts reported do not reflect the amounts actually received by our directors. Instead, these amounts reflect the aggregate grant date fair values of share options and restricted share units granted to our directors during the year ended December 31, 2023, as computed in accordance with FASB ASC 718. Assumptions used in the calculation of these amounts are included in Note 13 to our audited financial statements included in our Annual Report on Form 10-K for the fiscal 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 directors 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.
(2) The aggregate number of shares subject to outstanding share options units held by each of our non-employee directors as of December 31, 2023 were as follows: Mr Ahrens: 0; Mr Chin: 0; Dr. Dunne 13,742; Ms. Hecht 0; Mr. Hunt: 43,886; and Mr. Kelly: 51,850.
(3) No outstanding restricted share units were held by our non-employee directors as of December 31, 2023.
(4) Represents consulting fees incurred in connection with Dr. Dunne's consulting arrangement.
(5) Mr. Ahrens did not stand for re-election to our board of directors at our 2023 Annual General Meeting of Shareholders held on May 3, 2023 and his service as a director ceased on the date of such meeting.
(6) Mr. Chin resigned as a member of our board of directors on December 31, 2023.

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 annual general meeting of shareholders, it was resolved to pay a cash amount of $40,000 to the non-employee directors.

Consulting Agreement

During 2023, 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, Iterum Therapeutics International Limited ("ITIL"), dated May 25, 2022, (the "Consulting Agreement"), effective May 1, 2022. The 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 new drug application for oral sulopenem including the design and conduct of a Phase 3 clinical trial to support such resubmission. The Consulting Agreement was amended, effective December 31, 2022, to extend the term of the 2022 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 and again on December 27, 2023 to extend the term until June 30, 2024. An aggregate of $60,000 was expensed for services provided by Dr. Dunne in 2023 pursuant to the 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 annual general meeting of shareholders, it was resolved to pay a cash amount of $40,000 to the non-employee directors.

Clawback Policy

In October 2023, our Board adopted a written Compensation Recovery Policy ("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. Our Clawback Policy is set forth in an exhibit to the Company's Annual Report on Form 10-K for the fiscal year 2023. The Company did not have an accounting restatement in 2023.

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.

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.

EQUITY COMPENSATION PLANS AND OTHER BENEFIT PLANS

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, 2023. As of December 31, 2023, we had two equity compensation plans, the 2018 Equity Incentive Plan (the "2018 Plan"), and the 2015 Equity Incentive Plan, (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))
Equity compensation plans approved by shareholders	984,155	$ 2.18	133,140
Equity compensation plans not approved by shareholders	124,833 (1)	7.07	178,100
Total	1,108,988	2.73	311,240

(1) Represents share option awards and a restricted share unit award 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.

2021 Inducement Equity Incentive 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 nonstatutory share options, or NSOs, share appreciation rights, or SARs, restricted shares, restricted share units, or RSUs, performance-based share awards, and other share awards.

As of December 31, 2023, share options to purchase 124,833 ordinary shares were outstanding under our 2021 Inducement Plan, with a weighted-average exercise price of $7.07 per share. As of December 31, 2023, there were 16,666 ordinary shares to be issued upon vesting of outstanding RSUs.

2018 Equity Incentive 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, 2023, share options to purchase 976,657 ordinary shares were outstanding under our 2018 Plan, with a weighted-average exercise price of $1.82 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 executives; (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

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, 2023, share options to purchase 7,498 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, 2023.
- *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.

REPORT OF THE AUDIT COMMITTEE

In fulfilling its responsibilities for the financial statements for the fiscal year ended December 31, 2023, the audit committee took the following actions:

- reviewed and discussed the audited financial statements for the fiscal year ended December 31, 2023 with management and KPMG, our independent registered public accounting firm;
- discussed with KPMG the matters required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board ("PCAOB") in accordance with Auditing Standard No. 1301, Communications with Audit Committees, and the SEC;
- received the written disclosures and the letter from KPMG regarding its independence as required by applicable requirements of the PCAOB regarding KPMG's communications with the audit committee and has discussed with KPMG their independence; and
- considered the status of other areas of oversight relating to the financial reporting and audit process that the audit committee determined appropriate.

Based on the foregoing, the audit committee recommended to the board that the audited financial statements be included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2023 for filing with the SEC.

Audit Committee
David G. Kelly (Chairman)
Beth P. Hecht
Ronald M. Hunt
Mark Chin

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, 2023, were met.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions since January 1, 2022, 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 have engaged in the related party transactions described below. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, from unaffiliated third parties.

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, Iterum Therapeutics International Limited, 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.

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 and Share Award Letter

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 the 2021 Consulting Agreement with Dr. Dunne for the provision of general support and strategic advice in connection with our NDA. 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 2022 Consulting Agreement with Dr. Dunne, effective May 1, 2022, for the provision of general support and strategic advice in connection with the potential resubmission of the NDA for oral sulopenem including the design and conduct of a Phase 3 clinical trial to support such resubmission. The 2022 Consulting Agreement entitles Dr. Dunne to consulting fees of $5,000 per month. The 2022 Consulting Agreement was amended, effective December 31, 2022, to extend the term of the 2022 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 and again on December 27, 2023 to extend the term until June 30, 2024. An aggregate of $60,000 was expensed for services provided by Dr. Dunne in 2023 pursuant to the 2022 Consulting Agreement, as amended.

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.

MATTERS TO COME BEFORE THE ANNUAL GENERAL MEETING

PROPOSAL NO 1: ELECTION OF CLASS III DIRECTORS

Based upon the recommendation of the nominating and corporate governance committee of our board of directors, our board of directors has nominated Corey Fishman and Ronald Hunt for re-election at the AGM as Class III directors for a term of three years to serve until the 2027 annual general meeting of shareholders, subject to each such nominee's prior death, resignation, retirement, disqualification or removal.

Unless otherwise instructed in the proxy, all proxies will be voted "FOR" the election of the nominees identified above. Each of the nominees has indicated his or her willingness to serve on our board of directors, if elected. If any nominee should be unable to serve, the person acting under the proxy may vote the proxy for a substitute nominee designated by our board of directors. We do not contemplate that any of the nominees will be unable to serve if elected. Proxies cannot be voted for a greater number of persons than the number of nominees named in this proposal.

In order to be elected as a director, each nominee must receive the affirmative vote of a majority of the votes cast at the AGM.

OUR BOARD OF DIRECTORS RECOMMENDS THAT YOU VOTE FOR THE ELECTION OF COREY FISHMAN AND RONALD HUNT AS CLASS III DIRECTORS.

PROPOSAL NO. 2: TO RATIFY, IN A NON-BINDING VOTE, THE APPOINTMENT OF KPMG TO SERVE AS OUR INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM FOR THE FISCAL YEAR ENDED DECEMBER 31, 2024 AND TO AUTHORIZE THE BOARD OF DIRECTORS, ACTING THROUGH THE AUDIT COMMITTEE, TO SET THE INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM'S REMUNERATION.

The audit committee has appointed KPMG as our independent registered public accounting firm, to audit our financial statements for the fiscal year ending December 31, 2024. KPMG has served as our independent registered public accounting firm for the fiscal year ended December 31, 2024. Representatives of KPMG are expected to be present in person or telephonically at the AGM and will have the opportunity to make a statement if they desire to do so. It is also expected that they will be available to respond to appropriate questions from shareholders.

In deciding to appoint KPMG, the audit committee reviewed auditor independence issues and existing commercial relationships with KPMG and concluded that KPMG has no commercial relationship with the Company that would impair its independence for the fiscal year ending December 31, 2024.

The following table presents fees for professional audit services and other services rendered by KPMG to us for the fiscal years ended December 31, 2023 and 2022:

	December 31, 2023	December 31, 2022
Audit fees [1]	$ 258,000	$ 212,434
Audit related fees [2]	—	—
Tax fees [3]	64,762	48,430
All other fees	—	—
	$ 322,762	$ 260,864

(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.

Our board of directors is seeking shareholder ratification of the appointment by the audit committee of KPMG to serve as our independent registered public accounting firm and the authorization of the board of directors, acting through the audit committee, to set the auditor's remuneration. If this proposal is not approved at the AGM, our audit committee may reconsider this selection.

The affirmative vote of a majority of the votes cast at the AGM is required for this proposal.

OUR BOARD OF DIRECTORS RECOMMENDS THAT YOU VOTE FOR THE RATIFICATION OF THE APPOINTMENT OF KPMG AS OUR INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM FOR THE FISCAL YEAR ENDING DECEMBER 31, 2024 AND THE AUTHORIZATION OF THE BOARD OF DIRECTORS, ACTING THROUGH THE AUDIT COMMITTEE, TO SET THE AUDITOR'S REMUNERATION.

PROPOSAL NO 3: TO VOTE ON AN ADVISORY, NON-BINDING, RESOLUTION TO APPROVE THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS

We are providing our shareholders the opportunity to vote to approve, on an advisory, non-binding basis, the compensation of our named executive officers as disclosed in this proxy statement. This proposal, which is commonly referred to as "say-on-pay," is required by the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 (the "Dodd-Frank Act") which added Section 14A to the Exchange Act. Section 14A of the Exchange Act also requires that shareholders have the opportunity to cast an advisory vote with respect to whether future executive compensation advisory votes will be held every one, two or three years, which is the subject of Proposal 4.

Our executive compensation programs are designed to attract, motivate and retain our executive officers, who are critical to our success. Under these programs, our named executive officers are rewarded for the achievement of our short-term and longer-term financial and strategic goals.

The "Executive and Director Compensation" section of this proxy statement describes in detail our executive compensation programs and the decisions made by our compensation committee and board of directors. Highlights of our executive compensation program include the following:

- Competitive, market-based salaries, with annual adjustments;
- Cash bonuses, payable at the discretion of board and assessed on individual and company performance on an annual basis; and
- Equity awards to incentivize long-term value creation.

As we describe in the "Executive Officer and Director Compensation" section, our executive compensation program embodies a pay-for-performance philosophy that supports our business strategy and seeks to align the interests of our executives with our shareholders. The board believes this link between compensation and the achievement of our short-term and long-term business goals has helped drive our performance over time. At the same time, we believe our program does not encourage excessive risk-taking by management.

Our board of directors is asking shareholders to approve a non-binding advisory vote on the following resolution:

"**RESOLVED**, that the compensation paid to the Company's named executive officers, as disclosed pursuant to the compensation disclosure rules of the Securities and Exchange Commission, including the compensation discussion and analysis, the compensation tables and any related material disclosed in this proxy statement, is hereby approved."

As an advisory vote, this proposal is not binding. Neither the outcome of this advisory vote nor of the advisory vote included in Proposal 4 overrules any decision by us or our board of directors (or any committee thereof), creates or implies any change to our fiduciary duties or those of our Board of Directors (or any committee thereof), or creates or implies any additional fiduciary duties for us or our board of directors (or any committee thereof). However, our compensation committee and board value the opinions expressed by our shareholders in their vote on this proposal and will consider the outcome of the vote when making future compensation decisions.

OUR BOARD OF DIRECTORS RECOMMENDS THAT YOU VOTE TO APPROVE THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS BY VOTING FOR PROPOSAL NO. 3.

PROPOSAL NO 4: TO VOTE ON AN ADVISORY, NON-BINDING PROPOSAL ON THE FREQUENCY OF FUTURE ADVISORY VOTES ON THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS

In Proposal 3, we are providing our shareholders the opportunity to vote to approve, on an advisory, non-binding basis, the compensation of our named executive officers. In this Proposal 4, we are asking our shareholders to cast an advisory, non-binding, vote regarding the frequency of future advisory, non-binding, votes on the compensation of our named executive officers. As this is the first year in which we are required to hold an advisory vote on executive compensation pursuant to the SEC's rules, we do not currently have an established frequency for such votes.

Our board of directors will take into consideration the outcome of this vote in making a determination about the frequency of future advisory votes on the compensation of our named executive officers. However, because this vote is advisory and non-binding, our board of directors may decide that it is in our best interest and the best interests of our shareholders to hold the advisory vote to approve named executive officer compensation more or less frequently (but no less frequently than once every three years, as required by the Dodd-Frank Act). In the future, we will propose an advisory vote on the frequency of future advisory votes on the compensation of our named executive officers at least once every six calendar years as required by the Dodd-Frank Act.

After careful consideration, our board of directors believes that an advisory vote on executive compensation should be held every year. Therefore, our board of directors recommends that you vote for a frequency of one year for future executive compensation advisory votes.

Our board of directors believes that an annual executive compensation advisory vote will facilitate more direct shareholder input about the compensation of our named executive officers. An annual advisory vote on the compensation of our named executive officers is consistent with our policy of reviewing our compensation program annually. We believe an annual vote would be the best governance practice for our company at this time.

OUR BOARD OF DIRECTORS BELIEVES THAT HOLDING AN ANNUAL ADVISORY, NON-BINDING, VOTE ON THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS EVERY YEAR IS IN THE BEST INTERESTS OF THE COMPANY AND ITS SHAREHOLDERS AND RECOMMENDS THAT YOU VOTE FOR A FREQUENCY OF ONE YEAR.

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. Information contained on, or that can be accessed through, our website is not incorporated by reference into this document, and you should not consider information on our website to be part of this document.

OTHER MATTERS

The board of directors knows of no other business which will be presented to the AGM. If any other business is properly brought before the AGM, proxies will be voted in accordance with the judgment of the persons named therein.

Solicitation of Proxies

This proxy is solicited on behalf of our board of directors. We will bear the expenses connected with this proxy solicitation. In addition to the solicitation of proxies by mail, we expect to pay banks, brokers and other nominees their reasonable expenses for forwarding proxy materials and annual reports to principals and obtaining their voting instructions. In addition to the use of the mail, our directors, officers and employees may, without additional remuneration, solicit proxies in person or by use of other communications media. We have engaged Morrow Sodali LLC, or Morrow Sodali, to solicit proxies from shareholders in connection with the AGM. We will pay Morrow Sodali a fee of approximately $10,000, plus reasonable out of pocket fees and expenses for soliciting proxies. In addition, Morrow Sodali and certain related persons will be indemnified against certain liabilities arising out of or in connection with the engagement. Proxies may be solicited by Morrow Sodali by mail, telephone and e-mail.

Householding of Annual and Extraordinary Meeting Materials

Some banks, brokers and other nominee record holders may be participating in the practice of "householding" proxy statements and annual reports. This means that only one copy of our proxy statement, annual report, Irish Statutory Financial Statements or Notice of Internet Availability of Proxy Materials may have been sent to multiple shareholders in the same household. We will promptly deliver a separate copy of any such document to any shareholder upon request submitted in writing to us at Iterum Therapeutics plc, Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, Ireland, Attention: Investor Relations, or by calling +353 1 9038354. Any shareholder who wants to receive separate copies of the proxy statement, annual report, Irish Statutory Financial Statements or Notice of Internet Availability of Proxy Materials in the future, or who is currently receiving multiple copies and would like to receive only one copy for his or her household, should contact his or her bank, broker or other nominee record holder, or contact us at the above address and phone number.

Shareholder Proposals for 2025 Annual General Meeting of Shareholders

Proposals of shareholders intended to be presented at our 2025 annual general meeting of shareholders pursuant to Rule 14a-8 promulgated under the Exchange Act must be received by us at our offices at c/o Secretary, Iterum Therapeutics plc, Fitzwilliam Court, 1st Floor, Leeson Close, Dublin 2, Ireland, no later than December 27, 2024, in order to be included in the proxy statement and proxy card relating to that meeting.

In addition, shareholders who intend to present matters for action at our 2025 annual general meeting or nominate directors for election to our board of directors (other than pursuant to Rule 14a-8) must comply with the requirements set forth in our Constitution. For such matters under our Constitution, proper written notice must be received by our secretary at our registered office at the address noted above, no earlier than December 27, 2024 and no later than January 26, 2025; except if the date of the 2025 annual general meeting is changed by more than thirty (30) days from the first anniversary date of the 2024 Annual General Meeting, the shareholder's notice must be so received no earlier than one hundred and twenty (120) days prior to such annual general meeting and no later than the close of business on the later of (i) the 90th day prior to such annual general meeting or (ii) the 10th day following the day on which a public announcement of the date of the annual general meeting is first made.

In addition to satisfying the requirements of the advance notice provisions of our Constitution, shareholders who intend to solicit proxies in support of director nominees other than the Company's nominees at our 2025 annual general meeting must provide us with the information required by Rule 14a-19(b) under the Exchange Act.

Important Notice of the Internet Availability of Proxy Materials for the 2024 Annual General Meeting:

The Notice and Proxy Statement, Irish Statutory Financial Statements and 2023 annual report to shareholders are available at https://central.proxyvote.com/pv/web.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this proxy statement is considered to be part of this proxy statement. This proxy statement incorporates by reference the documents listed below (File No. 001-38503) that we previously filed with the SEC (other than those documents or the portions of those documents not deemed to be filed):

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2023.

A copy of our Annual Report on Form 10-K for the fiscal year ended December 31, 2023 may be obtained by shareholders without charge by written or oral request, or may be accessed on the Internet at https://www.sec.gov/.

You also may access these filings on our website at https://www.iterumtx.com/. Our website and the information contained on that site, or connected to that site, are not incorporated into this proxy statement.