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, 2020

OR

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

For the transition period from to

Commission File Number 001-38503

Iterum Therapeutics plc

(Exact name of Registrant as specified in its Charter)

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

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

Not applicable
(Zip Code)

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the Registrant's ordinary shares, $0.01 par value per share, on the Nasdaq Global Market on June 30, 2020, the last business day of the Registrant's most recently complete second fiscal quarter was $13,973,373.

The number of shares of Registrant's ordinary shares outstanding as of February 28, 2021 was 176,477,963.

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 2021 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, 2020.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

- our use of cash reserves;
- the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the potential advantages of our product candidates;
- the timing or likelihood of regulatory filings and approvals, including with respect to our new drug application for oral sulopenem for the treatment of uncomplicated urinary tract infections in patients with a quinolone non-susceptible pathogen;
- 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 continue as a going concern;
- the impact of COVID-19, including the responsive measures taken by governmental authorities and others, on our clinical trials, on regulatory approval, on future commercialization of, and future demand for, our products, available funding, our operations and the economy in general, which may precipitate or exacerbate other risks and/or uncertainties;
- our ability to maintain compliance with listing requirements of the Nasdaq Capital Market; 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.

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

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

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

This Annual Report also contains industry, market and competitive position data from our own internal estimates and research as well as industry and general publications and research surveys and studies conducted by third parties. Industry publications, studies, and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our internal data and estimates are based upon information obtained from trade and business organizations and other contacts in the markets in which we operate and our management's understanding of industry conditions. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal company research is reliable and the market definitions are appropriate, neither such research nor these definitions have been verified by any independent source. The industry in which we operate is subject to a high degree of uncertainty and risks due to various factors, including those described in the section titled "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 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, 2020, we had an accumulated deficit of $286.9 million.
- We will require additional capital to fund our operations and may be unable to obtain financing when needed or on acceptable terms.
- 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 U.S. Food and Drug Administration 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 sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing oral sulopenem, sulopenem or any other product candidate if such product candidate is approved.
- We 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 of oral sulopenem and sulopenem and expect to continue to do so in connection with any future commercialization and for any future clinical trials and commercialization of our product candidates and potential product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- We rely heavily on the exclusive license agreement with Pfizer Inc., or Pfizer, 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. 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.
- Our business, results of operations, financial condition, cash flows and share price can be adversely affected by pandemics, epidemics or other public health emergencies, such as the COVID-19 pandemic, which could delay our ability to complete our clinical trials, delay the initiation of our planned clinical trials and which may delay the initiation of future clinical trials, disrupt regulatory activities or have other adverse effects on our business and operations. In addition, the COVID-19 pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business and operations.

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. 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 all 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 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 (ASB) 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 ASB 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. Based on discussions with the FDA at a pre-New Drug Application, or 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. The FDA has designated our application as a priority review and consequently assigned a Prescription Drug User Fee Act, or PDUFA, goal date for completion of the review of oral sulopenem of July 25, 2021. The FDA currently plans to hold an advisory committee meeting on June 2, 2021 to discuss the NDA.

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

The treatment of urinary tract and intra-abdominal infections has become more challenging because of the development of resistance by pathogens responsible for these diseases. There are approximately 13.5 million emergency room and office visits for symptoms of urinary tract infections (UTIs) and approximately 21 million uUTIs in the United States annually, with approximately 30% of those infections caused by a quinolone non-susceptible organism. Based on market research, physicians estimated that

approximately 35% of these patients are at elevated risk for treatment failure. Proper antibiotic treatment of drug-resistant infections in this group is particularly important due to the risks associated with treatment failure. Elevated risk patients were defined in the research as patients with recurrent UTIs, elderly patients, patients who have a suspected or confirmed drug-resistant infection, patients with comorbidities (e.g., Diabetes mellitus) or that are immunocompromised, patients that have had a recent hospitalization, patients with a history of prior antibiotic failure and patients in a long-term care setting. Treatment failures pose significant clinical and economic challenges to the healthcare system. There are also approximately 3.6 million patients with cUTI and approximately 350,000 patients with cIAI that require antibiotic therapy every year in the United States.

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

None of the most commonly used oral antibiotics for treatment of uUTIs were initially approved by the FDA within the last two decades. We believe oral sulopenem will be an important 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 the FDA approves oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen, we expect to use a commercial partner to launch oral sulopenem in the United States. Data from an ongoing epidemiology study to quantify quinolone resistance by zip code, in addition to data from our clinical trials and available prescriber data, will inform our initial targeted sales force as to where the medical need for a new, effective therapy for UTIs is highest in the community setting. Outside of the United States, we are evaluating our options to maximize the value of our sulopenem program.

We registered two suppliers and validated one supplier for the manufacture of active pharmaceutical ingredient (API) for oral sulopenem at the time of our NDA filing. 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 28, 2021, we have exclusively licensed 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 oral sulopenem. We also own three U.S. patent applications (including one U.S. provisional patent application), two PCT patent applications, and nine 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.

In the third quarter of 2018 we initiated all three Phase 3 clinical trials, which were conducted under SPA agreements from the FDA and completed enrollment in the fourth quarter of 2019. Topline data from our cIAI trial readout in the fourth quarter of 2019 and showed that the primary endpoint was narrowly missed. In the cUTI trial, topline data was read out in the second quarter of 2020 and showed 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 ASB 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. 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 ASB 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. 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. The FDA has designated our application as a priority review and consequently assigned a PDUFA goal date for completion of the review of oral sulopenem of July 25, 2021.

Our Strategy

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

- ***Obtain regulatory approval for oral sulopenem in the United States.*** We submitted an NDA for oral sulopenem to the FDA and the FDA accepted the application for review in January 2021. The FDA has assigned a PDUFA goal date for completion of the review of oral sulopenem of July 25, 2021. The FDA currently plans to hold an advisory committee meeting on June 2, 2021 to discuss the NDA. We are considering the timing of a potential submission of a Marketing Authorization Application (MAA) to the EMA.
- ***Maximize commercial potential of our sulopenem program.*** If approved, we intend to use a third party to commercialize oral sulopenem in the United States with a targeted sales force in the community setting. Outside of the United States, we are evaluating our options to maximize the value of our sulopenem program.
- ***Pursue the development of oral sulopenem and sulopenem in additional indications.*** In the first half of 2021, we plan to request a meeting with the FDA to discuss the potential path to regulatory approval for cUTI, and depending on the outcome of that discussion, we may perform additional clinical development of sulopenem in cUTI. In the future, we may also pursue development of our sulopenem program in additional indications in adults and children, including community acquired bacterial pneumonia, bacterial prostatitis, diabetic foot infection and bone and joint infection, as well as new formulations to support these indications.
- ***Expand label for uUTI, if approved.*** If our pending NDA for the treatment of uUTI in patients with a quinolone non-susceptible pathogen is approved by the FDA, we plan to request a meeting with the FDA to discuss the required clinical development work for potential expansion of the label for uUTI to include all patients.
- ***Build a portfolio of differentiated anti-infective products.*** We intend to enhance our product pipeline through strategically in-licensing or acquiring clinical stage product candidates or approved products for the community and/or hospital and acute care markets. We believe that our focus on acute care in both the community and hospital markets will make us an attractive partner for companies seeking to out-license products or product candidates in our areas of focus.

The Medical Need

Urinary Tract and Intra-Abdominal Infections

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

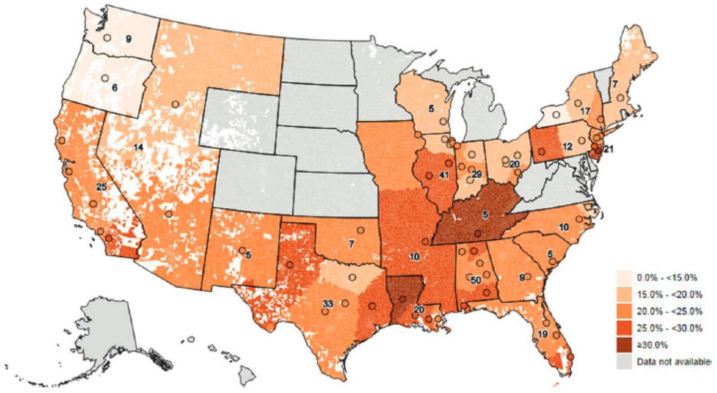
cIAIs have similar challenges to those of cUTIs. These complicated infections extend from a gastrointestinal source, such as the appendix or the colon, into the peritoneal space and can be associated with abscess formation.

Antimicrobial Resistance is Increasing

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

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

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



Numbers represent hospital centers from which data were derived

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

There is a Significant Population at Risk

There are approximately 13.5 million emergency room and office visits for symptoms of UTIs and approximately 21 million uUTIs in the United States annually with approximately 30% of those infections caused by a quinolone non-susceptible organism. Based on market research, physicians estimated that approximately 35% of these patients are at elevated risk for treatment failure. Proper antibiotic treatment of drug-resistant infections in this group is particularly important due to the consequences associated with treatment failure. Elevated risk patients were defined in the research as patients with recurrent UTIs, elderly patients, patients who have a suspected or confirmed drug-resistant infection, patients with comorbidities (e.g., Diabetes mellitus) or that are immunocompromised, patients that have had a recent hospitalization, patients with a history of prior antibiotic failure and patients in a long-term care setting.

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

Limited Treatment Options

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

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

The Challenge of Developing Antibiotics

Antibiotics work by targeting a critical function of the bacteria and rendering it non-functional. These critical functions include the ability to make proteins, to replicate further, and to build protective envelopes against the harsh external environment. These functions are coded in the bacteria’s DNA, which is copied over to each generation. Occasionally errors are made in the copying;

typically, these errors kill off the progeny but can sometimes actually help them survive under specific circumstances, namely when threatened by an antibiotic.

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

The Solution to Rising Resistance

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

These new agents will need to:

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

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

Our Sulopenem Program

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

Potential Advantages of Oral Sulopenem and Sulopenem

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

Sulopenem's differentiating characteristics include:

- ***Activity as an oral agent and favorable pharmacokinetic profile.*** Sulopenem is the active moiety with antibacterial activity. Oral sulopenem is a prodrug specifically selected among many other prodrug candidates because it enables the absorption of sulopenem from the gastrointestinal tract. It is this oral agent, sulopenem etzadroxil, combined with probenecid that we believe meets an urgent medical need to allow patients with resistant pathogens to be treated safely in the community, as well as allowing hospitalized patients to continue their treatment at home. Oral sulopenem is sufficiently absorbed from the gastrointestinal tract to allow the parent compound, sulopenem, to achieve adequate exposure in the tissues and, as demonstrated in animal models, to significantly reduce the burden of offending pathogens. Based on pharmacokinetic

modeling and supported by prior clinical data from Japan, we believe dosing of the oral agent twice daily will provide tissue exposure sufficient to resolve clinical infection.

- ***Targeted spectrum of activity against relevant pathogens without pressure on other incidental gram-negative organisms.*** Sulopenem is active against the pathogens that are most likely to cause infection of the urinary and gastrointestinal tract, including *E. coli*, *K. pneumoniae*, *P. mirabilis* and *B. fragilis*. Like ertapenem, sulopenem is not active against certain gram-negative organisms such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. These organisms are not typically seen in community UTIs and are infrequently identified in UTIs in the hospital, except when patients have had an indwelling urinary catheter for an extended duration. As a result, we believe the targeted spectrum of sulopenem is less likely to put pressure on those pathogens which could otherwise have led to carbapenem resistance.
- ***Activity against multidrug resistant pathogens.*** Bacteria are accumulating resistance mechanisms to multiple classes of antibiotics within the same organism, and, as a consequence, physicians are losing confidence in existing antibiotics as empiric therapy before culture results become available. Sulopenem is active against organisms that have multiple resistance mechanisms and can help avoid some of the consequences of ineffective antibiotic therapy.
- ***Documented safety and tolerability profile.*** 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, 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.
- ***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 registered 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 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 caused by a quinolone non-susceptible pathogen in the community. We estimate that approximately 30% of uUTIs in the United States are caused by quinolone non-susceptible pathogens, with the size of our initial market about 6-7 million infections annually.

In addition, we plan to request a meeting with the FDA to discuss the potential path to regulatory approval for the treatment of cUTI, and depending on the outcome of that discussion, we may perform additional clinical development of sulopenem in this indication. In the event the FDA approves our NDA for uUTI in patients with a quinolone non-susceptible pathogen currently under

review with the FDA, we plan to request a meeting with the FDA to discuss the required clinical development work for potential expansion of the label foruUTIs to include all patients.

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

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

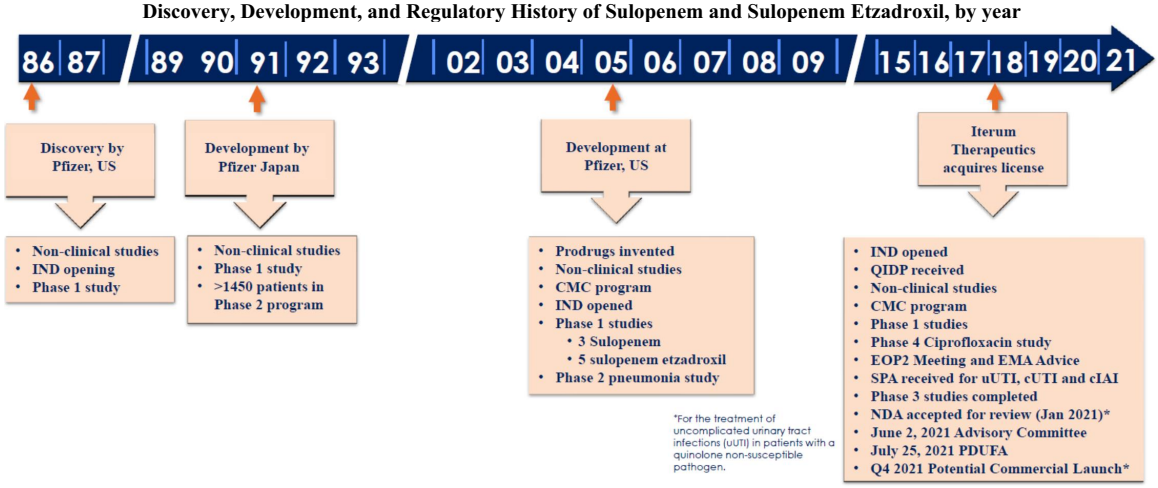
Given the growing prevalence of bacterial resistance that has rendered existing oral therapies ineffective, coupled with the FDA mandating new safety labeling changes to enhance warnings limiting fluoroquinolone use in uncomplicated infections due to the association with disabling and potentially permanent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

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

Oral Sulopenem and Sulopenem Clinical Development Program

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

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



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

Both sulopenem and oral sulopenem have received QIDP designation status for the indications of uUTI, cUTI and cIAI as well as for community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease. Fast track designation for these seven indications in both the oral and intravenous formulations has also been granted. QIDP designation status for other indications is also possible given the coverage of gram-negative and gram-positive bacteria by sulopenem, pending submission of additional documentation and acceptance by the FDA. We 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 nonclinical study requirements, the design of the Phase 1 and Phase 3 clinical trials, the pediatric development plan, as well as support for the proposed 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 ASB 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 ASB 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. The FDA has designated our application as a priority review and consequently assigned a PDUFA goal date for completion of the review of oral sulopenem of July 25, 2021. The FDA currently plans to hold an advisory committee meeting on June 2, 2021 to discuss the NDA.

We also have an agreement with the FDA on a pediatric study plan. Development work on pediatric formulations is ongoing, and we plan to commence Phase 1 trials in children in the first quarter of 2021.

Microbiology Surveillance Data

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

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

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

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

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

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

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

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

Animal Models

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

Non-clinical Pharmacology

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

Phase 1 Program

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

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

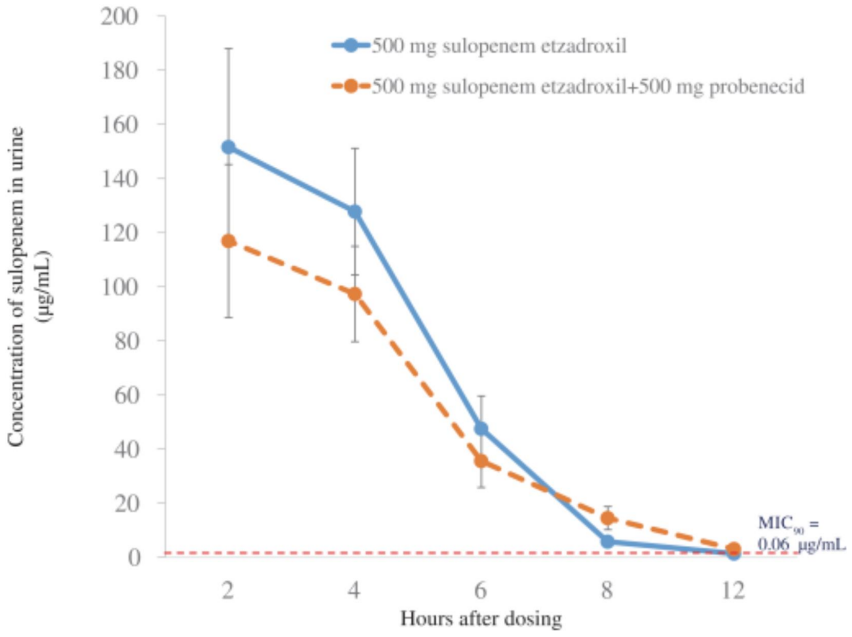
Oral Sulopenem

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



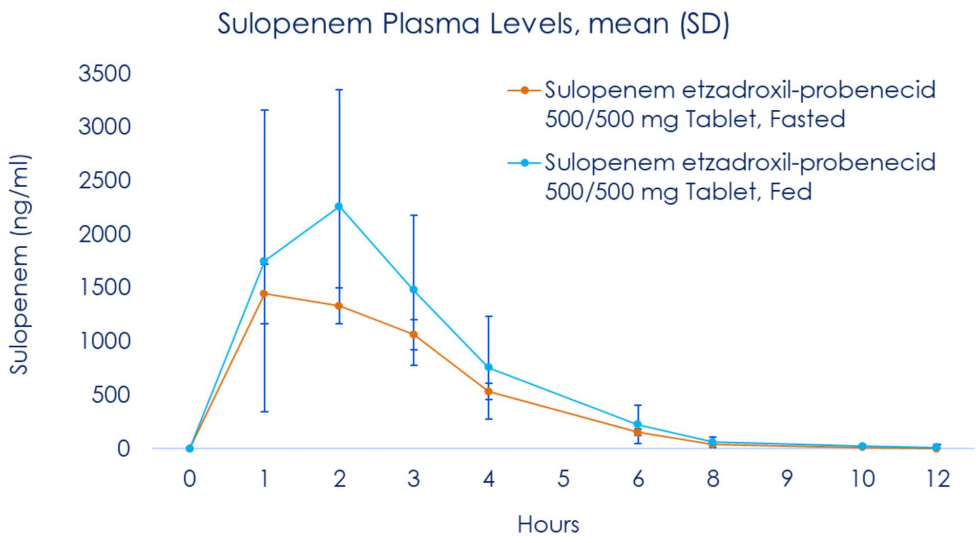
In IT001-102, we evaluated sulopenem etzadroxil administered with and without probenecid in a randomized cross-over trial in healthy volunteers in a fasted state. Subjects receiving sulopenem etzadroxil in a powder-in-a-bottle formulation co-administered with a separate tablet of probenecid demonstrated 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 $_{0-\infty}$ (hr*ng/mL)**	**T>MIC (0.5 µg/mL) [hr]**	**T>MIC (0.5 µg/mL) [%]**
500 mg Sulopenem etzadroxil	10	Mean	1928	3871	2.8	23.3
500 mg Sulopenem etzadroxil + 500 mg probenecid	11	Mean	1929	4964	3.6	30.2

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

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

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

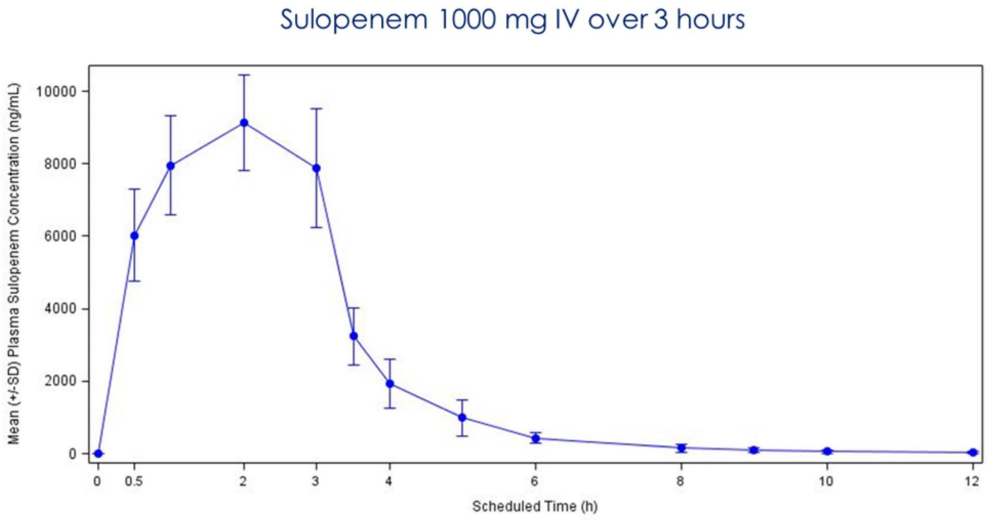
Doses of sulopenem up to 2800 mg as a single IV dose and 2000 mg BID, or twice daily, of sulopenem as IV over fourteen days were studied in three Phase 1 clinical trials in healthy adults, one study in patients with renal insufficiency in the United States and two Phase 1 clinical trials in Japan. Results 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 $_{0-\infty}$ (µg hr/mL)	$T_{1/2}$ (h)	CL_{total} (mL/min/kg)
Day 1	8	800	3	7.27	22.4	0.83		
	8	1200	1	32.5	42.3	1.04		
	8	1200	2.5	16.6	41.9	1.12		
Day 14	5	800	3	8.97	26.5	0.89		15.4
	6	1200	1	30.7	41.4	1.05		14.7
	6	1200	2.5	13.5	34.6	1.01		18.8

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

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

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



Modeling and Dose Selection

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

Japanese Clinical Data

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

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

Study #	Description	Sulopenem Dose	Comparator	N
91-002	Multiple infections in: Internal medicine Surgery: includes cIAI Urology: pyelonephritis cystitis	250 mg IV BID 500 mg IV BID	None	108

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

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

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

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

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

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

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

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

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

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

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

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

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

Phase 2 Clinical Trial with sulopenem and sulopenem etzadroxil

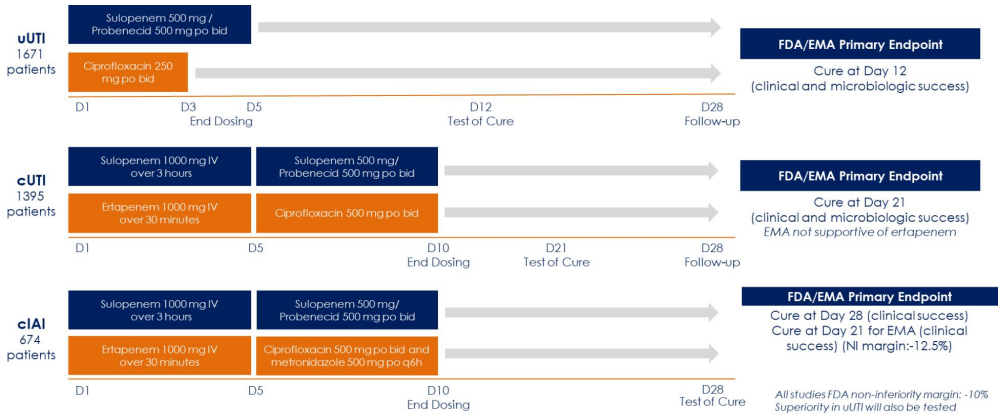
In 2009, Pfizer initiated a Phase 2, randomized, double-blind, double-dummy clinical trial in hospitalized patients with CAP comparing two regimens of IV sulopenem followed by sulopenem etzadroxil to ceftriaxone IV followed by amoxicillin-clavulanate. The sulopenem regimens were a single 600 mg IV dose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

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

Phase 3 Clinical Trials

Based on FDA Guidance from February 2015 (Complicated Intra-Abdominal Infections: Developing Drugs for Treatment. Guidance for Industry; Complicated Urinary Tract Infections: Developing Drugs for Treatment. Guidance for Industry) and on recently conducted studies by other sponsors, we negotiated SPA agreements for cUTI, cIAI and uUTI. All three Phase 3 clinical trials were initiated in the third quarter of 2018, and completed enrollment by the end of 2019. Oral sulopenem alone 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 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)

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 uUTI 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 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, or 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 ('CI') 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

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).

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 bothregimens, 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, 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.

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.

Pfizer License Agreement

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

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

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

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

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

Intellectual Property

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

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

Intellectual Property Relating to Oral Sulopenem

As of February 28, 2021, we have exclusively licensed 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 Hatch-Waxman Act to 2034, and three foreign patents related to oral sulopenem. We also own three U.S. patent applications (including one U.S. provisional patent application), two PCT patent applications, and nine 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 clinical development, including gepotidacin from GlaxoSmithKline, tebipenem pivoxil from Spero Therapeutics, Inc. and pivmecillinam from Utility Therapeutics Limited.

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 Allergan plc and Pfizer, Vabomere from Melinta Therapeutics, Inc., Zerbaxa from Merck

& Co., Zemdri from Cipla, Xerava from La Jolla Pharmaceutical Company, Recarbrio from Merck & Co, and Fetroja from Shionogi & Co., Ltd. In addition, Nabriva Therapeutics plc's Contepo is an IV-administered product candidate in late-stage clinical development intended to treat resistant gram-negative infections.

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

United States Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (FDCA) and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

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

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with good laboratory practices (GLP) regulations;
- submission to the FDA of an investigational new drug (IND) application which must become effective before human clinical trials may begin;
- approval by an independent institutional review board (IRB) at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices (GCPs) to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices (cGMP), and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;

- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of clinical data;
- payment of user fees and securing FDA review and approval of the NDA; and
- commitment to comply with any post-approval requirements and the potential requirement to conduct post-approval studies.

Preclinical Studies

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

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

Clinical Trials

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

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

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

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

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

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

clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Information about clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on its ClinicalTrials.gov website.

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 applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, 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 applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the Food and Drug Administration Safety and Innovation Act. The FDA maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In 2017, with passage of the FDA Reauthorization Act of 2017, Congress further modified these provisions. Previously, drugs that had been granted orphan drug designation were exempt from the requirements of the PREA. Under the amended section 505B, beginning on August 18, 2020, the submission of a pediatric assessment, waiver or deferral will be required for certain molecularly targeted cancer indications with the submission of an application or supplement to an application.

FDA Review and Approval 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 chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2021 is $2,875,842 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2021 is $336,432. The FDA granted us a small business waiver of the application fee in respect of our NDA for oral sulopenem based on its determination that we meet the statutory

requirements of the FDCA. Under the Prescription Drug User Fee Act (PDUFA) guidelines that arecurrently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision. Furthermore, the FDA is not required to complete its review within the established ten-month timeframe and may extend the review process by issuing requests for additional information or clarification.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy (REMS) plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools. The FDA provided written notice to us in February 2021 that there is currently no requirement for a REMS plan in connection with our NDA for oral sulopenem.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facilities in which it is manufactured, processed, packaged or held meet standards designed to assure the product's continued safety, quality and purity. In January 2021, the FDA accepted for review our NDA for oral sulopenem for the treatment of uUTIs in patients with a quinolone non-susceptible pathogen.

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 currently plans to hold an advisory committee meeting on June 2, 2021 to discuss our NDA.

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

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

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

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

Special FDA Expedited Review and Approval Programs

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

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need, or if the drug qualifies as a QIDP under the GAIN Act. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

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

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

Post-Approval Requirements

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

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

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

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

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

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

- restrictions on, or suspensions of, the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- interruption of production processes, including the shutdown of manufacturing facilities or production lines or the imposition of new manufacturing requirements;
- fines, warning letters or other enforcement letters or holds on post-approval clinical trials;

- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

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

Exclusivity and Approval of Competing Products

Hatch-Waxman Exclusivity

Market and data exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the activity of the drug substance. We believe that our product candidate under review, oral sulopenem, is a new chemical entity. 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 marketing protection to the term of any existing patent or non-patent regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA or biologics license application sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data does not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the 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.

Regulation Outside of the United States

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

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new legislation aims at simplifying and streamlining the approval of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one EU Member State will only be required to submit a single application for approval of a clinical trial to a reporting EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials. In January 2020, the website of the European Commission reported that the implementation of the new Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit which was conducted in December 2020, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The Clinical Trials Regulation becomes applicable six months after the European Commission publishes notice of this confirmation and has published an expected system "go live" in December 2021.

As in the United States, similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries.

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, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the

assessment report and related materials. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable by up to two years). On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom, as the UK legislation now has the potential to diverge from EU legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the United Kingdom in the long-term. The Medicines and Healthcare products Regulatory Agency has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the United Kingdom's regulatory position on medicinal products evolves over time.

General Data Protection Regulation

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

Pharmaceutical Coverage and Reimbursement

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

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

Reimbursement may impact the demand for, and/or the price of, any drug product which obtains marketing approval. Even if coverage is obtained for a given drug product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with those medications. Patients are unlikely to use a drug product, and physicians may be less likely to prescribe a drug product, unless

coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of the drug product. Therefore, coverage and adequate reimbursement is critical to new drug product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

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

In addition, it is expected that the increased emphasis on managed care and cost containment measures in the United States by third-party payors will continue and place further pressure on pharmaceutical pricing and coverage. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more drug products that gain regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

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

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

Other Healthcare Laws

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

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, in return for either the referral of an individual, or the purchase, leasing, furnishing or arranging for the purchase, lease or order of a good, facility, item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other hand. The

Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, (ACA) amended the intent requirement of the federal Anti-Kickback Statute, such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it;

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

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

Ensuring that business arrangements with third parties comply with applicable healthcare laws and regulations is costly and time consuming. If business operations are found to be in violation of any of the laws described above or any other applicable governmental regulations a pharmaceutical manufacturer may be subject to penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from governmental funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, additional reporting

obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of operations, any of which could adversely affect a pharmaceutical manufacturer's ability to operate its business and the results of its operations.

Healthcare Reform

In the United States, there have been, and continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect the future results of pharmaceutical manufacturers' operations. In particular, there have been and continue to be a number of initiatives at the federal and state levels that seek to reduce healthcare costs.

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 2030 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.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress 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 December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020. On February 10, 2021, the Biden Administration withdrew the Department of Justice's support for this lawsuit. A ruling by the Court is expected sometime this year. 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 rescinded those orders and 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.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, 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 drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. To those ends, President Trump issued five executive orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these orders will remain in force under the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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

certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare 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 healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Commercialization Strategy and Organization

Given our stage of development, we have not yet established a commercial organization or distribution capabilities for our initial indication. If approved, we intend to commercialize our sulopenem program in the United States with a commercial partner with a targeted sales force in the community setting.

We have engaged a leading provider of commercial services to the life science industry to initiate pre-launch activities for oral sulopenem, followed by planned commercialization services upon final agreement. Prior to potentially receiving marketing approval of our NDA currently under FDA review, we plan to develop 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. We plan to accomplish this through a multi-faceted electronic campaign. Additionally, prior to potential commercial launch of oral sulopenem for the treatment of uUTI in patients with a quinolone non-susceptible pathogen, if approved, we plan to develop marketing, sales and training materials as well as begin interacting with physicians to discuss the uUTI disease state and challenges that the existing treatments are facing.

If our NDA is approved, we plan to work with our third-party provider to build a fully integrated commercial infrastructure to launch oral sulopenem in the United States. The commercial infrastructure would be led operationally by highly experienced management personnel and 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 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.

We expect our sales team to focus its efforts on the physicians in the community and we 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 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 will 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 increases, we would plan to broaden our target audience and geography by increasing the number of sales representatives to capture a larger percentage of the market.

We plan to 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 our 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 four third-party contract manufacturers for all of our required raw materials, drug substance, and finished drug product for our preclinical research and clinical trials. As of February 28, 2021, we had a 2-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 at the time we submitted our NDA, 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 28, 2021, we had 7 full-time employees, including a total of two employees with M.D. or Ph.D. degrees. We are also supported by consultants and contractors in most areas of the business, including clinical, regulatory, CMC, Quality Assurance and finance and business and operations support. Four 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. If we receive approval for oral

sulopenem, we may increase our workforce to supportcommercialization activities, and, if we pursue additional clinical work related to cUTI and/or 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 Block 2 Floor 3, Harcourt Centre, Harcourt Street, Dublin 2, Ireland, and our telephone number is (+353) 1 903-8920.

Available Information

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

Item 1A. Risk Factors.

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K and in other documents that we file with the 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 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, 2020, we had an accumulated deficit of $286.9 million and cash and cash equivalents of $14.5 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. The FDA has assigned a PDUFA (Prescription Drug User Fee Act) goal date for completion of the review of oral sulopenem of July 25, 2021.

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 financing arrangements 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 202((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) 6.500% Exchangeable Senior Subordinated Notes due 2025 (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 (the 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 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 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 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 approximately $17.4 million and net proceeds of approximately $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 shares (February 2021 Underwritten Offering), ordinary shares for aggregate gross proceeds to us of approximately $46.0 million and net proceeds of approximately $42.1 million after deducting fees payable to the underwriter and other estimated 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 approximately $35.0 million and net proceeds of approximately $32.2 million after deducting fees payable to the placement agent and other estimated offering expenses payable by us. Through February 28, 2021, net proceeds of $15.1 million have been received from the exercise of certain warrants issued as part of the June 30 Offering and October 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.

We expect to continue to incur significant expenses and increasing operating losses as we seek potential marketing approval for oral sulopenem, carry out pre-commercialization activities, potentially launch oral sulopenem and pursue the development of our sulopenem program in additional indications through preclinical and clinical development. Our expenses will also increase substantially if and as we:

- conduct additional clinical trials for oral sulopenem and/or sulopenem, which include our planned Phase 1 clinical trials related to pediatric indications;
- initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates;
- establish 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 sulopenemand/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 as we seek potential marketing approval for oral sulopenem, carry out pre-commercialization activities, and pursue the development of our sulopenem program in additional indications through preclinical and clinical development. If we obtain marketing approval for oral sulopenem, sulopenem or any future product candidate 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.

Based on our current operating plan, we estimate that our existing cash and cash equivalents as of December 31, 2020, together with the net proceeds of approximately $74.3 million from the February 2021 Underwritten Offering and February 2021 Registered Direct Offering, should be sufficient to fund our operating expenses and capital expenditure requirements into the first half of 2023, including through the PDUFA goal date of July 25, 2021 for completion of the FDA's review of the NDA for oral sulopenem for the treatment of uUTI in patients with quinolone-non-susceptible pathogens and the potential commercial launch of oral sulopenem. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plans may change as a result of many factors and various risks and uncertainties.

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. 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.

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 of regulatory review and potential approval of our pending NDA for oral sulopenem for the treatment of uUTI in patients with a quinolone non-susceptible pathogen;
- the timing and costs of our clinical trials of oral sulopenem and sulopenem, including our planned Phase 1 clinical trials related to pediatric indications and any other studies which may be required for regulatory approval of our product candidates;
- the initiation, progress, timing, costs and results of preclinical studies and clinical trials of other potential product candidates and of our current product candidates in additional indications;
- the amount of funding that we receive under government awards that we have applied for or may apply for in the future;
- the number and characteristics of product candidates that we pursue;

- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for oral sulopenem and/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;
- 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 the COVID-19 pandemic on the economy and our business generally including the impact the pandemic may have on timing of regulatory approval and commercialization of any future products; 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.

Provisions in the EN Indenture, RLN Indenture and our other financing documents may deter or prevent us from raising additional capital to fund our operations.

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 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.

In connection with the February 2021 Underwritten Offering, we entered into an Underwriting Agreement (the Underwriting Agreement) on February 3, 2021 with the underwriter. The Underwriting Agreement contains certain covenants, including covenants prohibiting the issuance of our ordinary shares or securities convertible or exchangeable into our ordinary shares for a period of 60 days after the closing of the February 2021 Underwritten Offering and prohibiting us from entering into variable rate transactions for a period of 12 months after the closing of the February 2021 Underwritten Offering, subject to certain exceptions. In addition, in connection with the June 3 Offering, the June 30 Offering, the October Offering, and the February 2021 Registered Direct Offering, we entered into securities purchase agreements which contain certain covenants, including prohibiting us from entering into variable rate transactions for a period of 12 months after the closing of the respective offerings, subject to certain exceptions. These and other provisions in the financing documents could deter or prevent us from raising additional capital. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to develop and commercialize our sulopenem program and otherwise pursue our business strategy.

We are heavily dependent on the success of our sulopenem program, and our ability to develop, obtain marketing approval for and successfully commercializeoral 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 depends 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:

- enrolling and successfully completing our planned Phase 1 clinical trials related to pediatric indications and any other 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, 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.

On April 27, 2018, our subsidiaries, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited (Borrowers), entered into a secured credit facility with SVB pursuant to which SVB agreed to lend the Borrowers up to $30.0 million in two term loans. $15.0 million of the secured credit facility was funded on closing and the other $15.0 million was available at our option upon the satisfaction of certain draw requirements. However, we did not satisfy the second draw conditions before the deadline of October 31, 2019. Obligations under the secured credit facility are secured by substantially all of our existing and future assets and the existing and future assets of our subsidiaries, including intellectual property. Our secured credit facility imposes operating and other restrictions on us. Such restrictions affect, and in many respects limit or prohibit, our ability to, among other things, dispose of certain assets, pay dividends and incur additional indebtedness. Failure to make payments or comply with these and other terms and covenants under our secured credit facility could result in an event of default, which could lead to an acceleration of amounts due and foreclosure upon and/or sale or other liquidation of all of our and our subsidiaries' assets, including intellectual property. Any of the foregoing would have a material adverse effect on our operations and financial condition. In addition, this indebtedness and the security interests granted to secure it could make it more difficult for us to raise additional capital to fund our operations.

In 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.

In addition, the EN Indenture and the RLN Indenture each contain affirmative and negative covenants which impose operating and other restrictions on us, including, among other things, incurring any indebtedness that is not permitted by the EN Indenture or

amending the terms of any subordinated indebtedness, entering into strategic transactions or transferring any material assets and undergoing a change of control transaction (subject to certain exceptions, including in the case of a change of control transaction, a transaction in which each holder of an outstanding Exchangeable Note receives cash consideration of at least 300% of the outstanding principal amount of such Exchangeable Note). Failure to comply with these terms could result in an event of default which could lead, among other things, to an acceleration of amounts due under the EN Indenture and the obligation to pay default interest. Moreover, obtaining a consent to a waiver of these terms is subject to a veto right of the holders of 30% of the outstanding Exchangeable Notes, in the case of the EN Indenture, and 30% of the outstanding RLNs, in the case of the RLN Indenture, and 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 October Offering, the exchange rate of the Exchangeable Notes increased and the exchange price of the Exchangeable Notes adjusted from the previous exchange price of $1.00 per ordinary share (at the exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes) to $0.7775 per ordinary share (at an adjusted exchange rate of 1,286.1845 shares per $1,000 of principal and interest on the Exchangeable Notes). As of February 28, 2021, approximately $16.2 million aggregate principal amount of Exchangeable Notes remained outstanding. 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 or to refinance our secured credit facility and the Exchangeable Notes, or to make cash payments, if we so elect, in connection with any exchange of Exchangeable Notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow sufficient to service our term loan, the Exchangeable Notes or other indebtedness and make necessary capital expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring indebtedness or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our term loan, the Exchangeable Notes or other indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

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

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

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

Holders of the Exchangeable Notes will have the right to require us to repurchase all or a portion of their 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. In addition, our ability to repurchase or to pay cash upon exchange of the Exchangeable Notes may be limited by law, regulatory authority, the Loan and Security Agreement and future indebtedness.

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

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

Beginning January 21, 2021 and prior to the earlier of (i) the close of business on the scheduled trading dayimmediately 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) theclose 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 ourexchange 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, whichcould 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.

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.

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.

We have filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on July 16, 2019 (File No.333-232569), and pursuant to which we registered for sale up to $150.0 million of any combination of our ordinary shares, preferred shares, debt securities, warrants and/or units from time to time and at prices and on terms that we may determine. The extent to which we are able to utilize the 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 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. As of February 28, 2021, we had issued $98.1 million of securities registered under our universal shelf registration statement.

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 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 pre-clinical 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 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 superiority to ciprofloxacin, 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. The FDA has assigned a PDUFA goal date for completion of the review of oral sulopenem of July 25, 2021. The FDA currently plans to hold an advisory committee meeting on June 2, 2021 to discuss the NDA. However, 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 sulopenem for this 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.

Risks Related to Clinical Development and Commercialization

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

We currently have no products approved for sale and have invested substantially all of our efforts and financial resources in the development of our sulopenem program. 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:

- completion of clinical trials, including our planned Phase 1 clinical trials related to pediatric indications and any other clinical trials that may be required for regulatory approval of our product candidates;
- successful enrollment in, and completion of, our planned Phase 1 clinical trials related to pediatric indications and any other 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. The FDA has designated our application as a priority review and consequently assigned a PDUFA goal date for completion of the review of oral sulopenem of July 25, 2021. The FDA currently plans to hold an advisory committee meeting on June 2, 2021 to discuss the NDA. However, due to a variety of factors, including those described in this "Risk Factors" section, we may nonetheless be ultimately unable to obtain FDA approval for sulopenem for this or any other indication or 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 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. The FDA has assigned a PDUFA goal date for completion of the review of oral sulopenem of July 25, 2021. The FDA currently plans to hold an advisory committee meetingon June 2, 2021 to discuss the NDA.

It is possible that the FDA may conclude after review of our data that our application is insufficient to obtain regulatory approval for any current or future product candidates. If the FDA does not approve our planned NDA, it may require that we conduct additional costly clinical, non-clinical or manufacturing validation studies before it will reconsider our application(s). Depending on the extent of these or any other FDA-required studies, approval of any NDA(s) or other application that we submit may be significantly delayed, possibly for several years, or may require us to expend more resources than we have available.

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, which was accepted by the FDA for review in January 2021, we have not previously submitted an NDA to the FDA or similar applications to comparable foreign regulatory authorities for any of our product candidates.

Our business currently 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. 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. The FDA has assigned a PDUFA goal date for completion of the review of oral sulopenem of July 25, 2021 and currently plans to hold an advisory committee meeting on June 2, 2021 to discuss the 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 Phase 3 clinical trials pursuant to Special Protocol Assessment (SPA) agreements and the FDA accepted our NDA application for review in January 2021, the FDA or other comparable foreign regulatory authorities may ultimately disagree as to the design or implementation of our Phase 3 clinical trials or other clinical trials;
- we may not reach agreement on acceptable terms with all clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different trial sites;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the FDA, the local National Health Authorities or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have to suspend or terminate clinical trials of a product candidate for various reasons, including non-compliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we enter into agreement for clinical and commercial supplies; or
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

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

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

Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of oral sulopenem, sulopenem or any other product candidate.

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

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

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for participation in the clinical trial;
- the number of sites at which we conduct the trial and the speed at which we are able to open such sites;
- the prevalence of antibiotic resistance to pathogens where we conduct the clinical trial;
- the accuracy of certain estimates and assumptions upon which the design of the protocols are predicated;
- our ability to recruit clinical trial investigators with appropriate experience;
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications that we are investigating;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before completion; and
- the impact on access to hospitals and willingness of patients to participate in clinical trials such as our planned Phase 1 clinical trials related to pediatric indications and any other clinical trials that may be required for regulatory approval of our product candidates, as a result of pandemics, like COVID-19, and other health crises.

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.

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, such as our planned Phase 1 clinical trials related to pediatric indications, 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 or the impact of pandemics, like COVID-19, to their business.

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 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

superiority to ciprofloxacin, sulopenem did not meet the primary endpoint of statistical non-inferiority comparedto ciprofloxacin in the population of patients with baseline pathogens susceptible to ciprofloxacin in our 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. It is possible that the FDA may conclude after review of our data that our application is insufficient to obtain regulatory approval for any current or future product candidates. 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. During the development of oral sulopenem and sulopenem, patients have experienced drug-related side effects including diarrhea, temporary increases in hepatic enzymes, allergic reactions, and rash. In the Japanese program conducted by Pfizer in the early 1990s, one patient reported a serious adverse event related to sulopenem of a transient elevation in liver function tests. The patient died due to metastatic lung cancer. Other serious adverse events recorded in patients receiving sulopenem in the Japanese program, which were not considered by the investigator to be related to sulopenem, included myocardial infarction with respiratory failure and progression of underlying ovarian carcinoma, in both cases resulting in death. For each of these patients, sulopenem was not determined to be the cause of death.

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, 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.

While we believe these results support a positive safety and tolerability profile for sulopenem, in future trials there may be unforeseen serious adverse events or side effects that differ from those seen in our 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.

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

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

We are currently evaluating our commercialization strategy in the United States and other territories. We are focusing our initial commercial efforts on the United States market, which we believe represents the largest market opportunity for our sulopenem program. We currently do not have a sales, marketing or distribution infrastructure and we have no experience in the sales, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either build our marketing, sales, distribution, managerial and other non-technical capabilities, or make arrangements to outsource those functions to third parties. If oral sulopenem and/or sulopenem receive 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 and/or sulopenem through collaboration arrangements. We are not currently party to any such arrangements but have engaged a potential commercial partner for commercialization services in the U.S. market and this commercial partner has initiated pre-launch activities. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we intend to target. If we are unable to establish a sales force and marketing and distribution capabilities, our operating results may be adversely affected. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of our product candidates.

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

- challenges in developing a commercialization strategy or launching new drug products using a traditional marketing model during a global health crisis or pandemic, like COVID-19;
- our inability to recruit 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;

- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- costs and expenses associated with creating an independent sales and marketing organization.

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

Furthermore, we may be unsuccessful in entering into the necessary arrangements or definitive agreements with third parties, including with respect to the potential commercialization of oral sulopenem in the United States, if approved, or in obtaining all necessary approvals that may be required to enter into such arrangements, or may be unable to do so on terms that are favorable to us. In addition, we likely would have little control over such third parties, and any of them might fail to devote the necessary resources and attention to sell and market our products effectively.

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

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

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

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

There are also a number of oral product candidates in clinical development by third parties that are intended to treat UTIs. Some mid- to late-stage product candidates include gepotidacin from GlaxoSmithKline, tebipenem pivoxil from Spero Therapeutics, Inc. 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 Allergan plc and Pfizer, Vabomere from Melinta Therapeutics, Inc., Zerbaxa from Merck & Co., Zemdri from Cipla, Xerava from La Jolla Pharmaceutical Company, Recarbrio from Merck & Co, and Fetroja from Shionogi & Co., Ltd. In addition, Nabriva Therapeutics plc's Contepo is an IV-administered product candidate in late-stage clinical development intended to treat resistant gram-negative infections.

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 for certain breakthrough devices, and under this policy, a QIDP product will be considered new and will not need to demonstrate that it meets the substantial clinical improvement criterion. Instead it will only need to meet the cost criterion. CMS has also increased the new technology add-on payment percentage to 75 percent for an antimicrobial designated by the FDA as a QIDP. The potential impact of this rule on sulopenem has not yet been assessed. On January 21, 2020, CMS updated its billing guidance on changes to new technology add-on payments for innovative antibiotics.

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Dependence on Third Parties

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

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

The Pfizer License gives us exclusive worldwide rights to develop, manufacture, and commercialize sulopenem etzadroxil and sulopenem, or any other prodrug of sulopenem previously identified by Pfizer as well as the right to use relevant information and regulatory documentation developed by Pfizer to support any regulatory filing worldwide. In exchange for those rights, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop, obtain regulatory approval for and commercialize sulopenem etzadroxil and sulopenem by implementing a specified development plan and providing an update on progress on an annual basis. Under the Pfizer License, we paid Pfizer a one-time non-refundable upfront fee of $5.0 million, clinical milestone payments totaling $15.0 million, upon first patient dosing of oral sulopenem and sulopenem in a Phase 3 clinical trial, and are obligated to pay Pfizer milestone payments upon the achievement of other specified regulatory and sales milestones as well as royalties ranging from a single-digit to mid-teens percentage based on the amount of marginal net sales of each licensed product. Pfizer also received 381,922 of our Series A preferred shares (which converted to ordinary shares in connection with our 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 have engaged a potential commercial partner for commercialization services in the U.S. market and this commercial partner has initiated pre-launch activities. The EN Indenture and RLN Indenture each contain restrictions on entering into collaborations requiring consent of a portion of the holders of each of the Exchangeable Notes and RLNs. There is no guarantee that we would be able to obtain such consent.

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

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

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

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

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

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

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

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

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

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

We do not have the internal infrastructure or capability to manufacture oral sulopenem and sulopenem for use in the conduct of our preclinical research or clinical trials 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 although negotiations are well advanced. If any of our existing manufacturers should become unavailable to us for any reason, we may incur delays in identifying or qualifying replacements.

We will enter into agreements with third-party contract manufacturers for the commercial production of oral sulopenem and/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 the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our drug candidates and jeopardize our ability to commence sales and generate revenue.

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

Risks Related to Our Intellectual Property

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

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

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

prospects. Disputes may arise regarding intellectual property subject to the Pfizer License or any of our future license agreements, including:

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

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

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

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

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

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

The patent position of pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of countries outside the United States may not protect our rights to the same extent as the laws of the United States. For example, 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). Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our patent rights may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

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

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

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

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

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

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

- we may not develop additional proprietary technologies that are patentable

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

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

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

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

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

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

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

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

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

Competitors may infringe, misappropriate or otherwise violate our patents, trademarks, copyrights or other intellectual property or those of our licensors. To counter infringement, misappropriation, unauthorized use or other violations, we may be required to file legal claims, which can be expensive and time consuming and divert the time and attention of our management and scientific

personnel. We may not be able to prevent, alone or with our licensors, infringement, misappropriation or other violations of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Trade secrets and know-how can be difficult to protect as trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. If we fail to prevent material disclosure of the know-how, trade

secrets and other intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition. Even if we are able to adequately protect our trade secrets and proprietary information, our trade secrets could otherwise become known or could be independently discovered by our competitors. For example, competitors could purchase our products and attempt to replicate some or all of the competitive advantages we derive from our development efforts, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, in the absence of patent protection, we would have no right to prevent them, or those to whom they communicate, from using that technology or information to compete with us.

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

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

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

In addition, any proprietary name we propose to use with oral sulopenem, sulopenem or any other product candidate in the United States must be approved by the FDA, and in Europe by the EMA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA and the EMA each typically conduct a review of proposed product names, including an evaluation of potential for confusion with other product names. While we have submitted our proposed proprietary name for oral sulopenem in connection with our NDA for oral sulopenem, 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 contract research organizations to assist us in this process.

Although we have QIDP status and fast track designation for sulopenem and oral sulopenem for the indications of uUTI, cUTI and cIAI (and for the indications of community-acquired bacterial pneumonia, acute bacterial prostatitis, gonococcal urethritis, and pelvic inflammatory disease) which may provide for a more rapid 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. In addition, the COVID-19 pandemic could impact the FDA's regulatory review process, including delays in meetings related to planned or completed clinical trials and ultimately the review and approval of our product candidates. 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 thatwe 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 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, the FDA may still require us to conduct additional non-clinical studies or clinical trials for our product candidates either prior to or post-approval, and it may otherwise object to elements of our clinical development program.

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

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

Of the large number of drugs in development, only a small percentage complete the FDA or foreign regulatory approval processes and are successfully commercialized. The lengthy review process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval, which would significantly harm our business, financial condition, results of operations and growth prospects. The FDA plans to hold an advisory committee meeting for oral sulopenem on June 2, 2021.

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

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

The FDA has established regulations to govern the drug development and approval process, as have foreign regulatory authorities. The policies of the FDA and other regulatory authorities may change and additional laws may be enacted or government regulations may be promulgated that could prevent, limit, delay, or alternatively accelerate regulatory review of our product candidates. Further, disruptions at the FDA and other agencies may prolong the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown 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. The Trump Administration also took several executive actions that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities.

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

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

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

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020 and a transition period to December 31, 2020, was established to allow the United Kingdom and the European Union to negotiate the United Kingdom's withdrawal. As a result, effective January 1, 2021, the United Kingdom is no longer part of the European Single Market and European Union Customs Union. A co-operation agreement was signed between the United Kingdom and the European Union in December 2020 which has been applied provisionally since January 1, 2021 until it is ratified by all parties to that agreement. The agreement addresses trade, economic arrangements, law enforcement, judicial cooperation and a governance framework including procedures for dispute resolution, among other things. As both parties continue to work on the rules for implementation, significant political and economic uncertainty remains about how the precise terms of the relationship between the parties will differ from the terms before withdrawal.

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

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

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

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

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

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

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

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

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

As a pharmaceutical company, even though we do not provide healthcare services or receive payments directly from or bill directly to Medicare, Medicaid or other third-party payors for our products, certain federal and state healthcare laws and regulations pertaining to fraud and abuse, patients' rights and other healthcare laws and regulations, are applicable to our business. We are subject

to healthcare laws and regulations by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

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

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

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

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

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

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

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

- establishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending; and
- implementation of the federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act."

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional congressional action is taken. The Coronavirus Aid, Relief, and Economic Security (CARES) Act suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030. 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.

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 December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020. On February 10, 2021, the Biden Administration withdrew the federal government's support for overturning the ACA. A ruling by the Court is expected sometime this year. 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. This executive order also directs the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic.

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. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

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 is 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. To date, 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 drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for products. To those ends, President Trump issued several executive orders intended to lower the costs of prescription drug products. Certain of these orders are reflected in recently promulgated regulations, including an interim final rule implementing President Trump's most favored nation model, but such final rule is currently subject to a nationwide preliminary injunction. It remains to be seen whether these orders and resulting regulations will remain in force during the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care 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.

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.

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 ofcertain 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. For example, our chief scientific officer resigned in December 2020 and transitioned to a consulting role and member of our board of directors. 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, particularly with the impact of the COVID-19 pandemic on the global workforce, 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, 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. For example, in 2020, we experienced a significant reduction in workforce as our initial sulopenem development program concluded. If we receive approval for oral sulopenem, we may increase our workforce to support commercialization activities, and, if we pursue additional clinical work related to cUTI and/or other indications, we may increase our research and development headcount.

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, like COVID-19; 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.

Our business, results of operations, financial condition, cash flows and share price can be adversely affected by pandemics, epidemics or other public health emergencies, such as the COVID-19 pandemic, which could delay our ability to complete our clinical trials, delay the initiation of our planned clinical trials and which may delay the initiation of future clinical trials, disrupt regulatory activities or have other adverse effects on our business and operations. In addition, the COVID-19 pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business and operations.

Our business, results of operations, financial condition, cash flows andshare price may be adversely affected by pandemics, epidemics or other public health emergencies, such as the recent outbreak of COVID-19 which has spread from China to many other countries, including the United States and Ireland. In March 2020, the World Health Organization characterized COVID-19 as a pandemic, and the President of the United States declared the COVID-19 outbreak a national emergency. The outbreak has resulted in governments around the world implementing increasingly stringent measures to help control the spread of the virus, including quarantines, "shelter in place" and "stay at home" orders, travel restrictions, business curtailments, school closures, and other measures. These responsive measures have had a significant impact, both direct and indirect, on business and commerce worldwide, as worker shortages have occurred, supply chains have been disrupted, and facilities and production have been suspended.

The COVID-19 pandemic may negatively affect our business and operations in a number of ways, and its long-term effects are uncertain. The spread of COVID-19 and the responsive measures taken to date have limited our access to our facilities and caused the majority of our employees to work from home. Responsive measures to COVID-19 have resulted in restrictions on operations at clinical trial sites which could impact the initiation of patient enrolment for our planned Phase 1 clinical trials related to paediatric indications. In addition, the COVID- 19 pandemic could impact the FDA's regulatory review process, including delays in meetings related to planned or completed clinical trials and ultimately the review and approval of our product candidates. The FDA's review of our pending NDA for oral sulopenem for the treatment of uUTI may be delayed due to COVID-19, including an inability to schedule, or delays in scheduling, meetings and inspections. Additionally, the COVID-19 pandemic may negatively impact our ability to initiate or complete future clinical trials, disrupt our regulatory and commercialization activities, and result in other adverse effects on our business and operations. For example, current and future restrictions on in-person interactions may impact how we commercialize our product candidates, if approved, and we may need to apply non-traditional marketing methods, which may ultimately not be efficient or successful.

In addition, our suppliers and manufacturers located in countries that have been affected by COVID-19 may also be disrupted, which may affect our ability to procure items that are essential for our research and development activities or commercialization in the event any of our product candidates is approved, and may cause disruptions in our current or future trials or commercialization activities. The response to the COVID-19 pandemic may redirect resources with respect to regulatory matters in a way that would adversely impact our ability to progress regulatory approval. We may also face impediments to regulatory meetings and approvals due to measures intended to limit in-person interactions. Additionally, we may also choose to redirect our own resources in a way that may adversely impact or delay certain of our programs.

We cannot foresee if and when the outbreak of COVID-19 will be effectively contained, nor can we predict the severity and duration of its impact. If the COVID-19 pandemic is not effectively and timely controlled, we may experience prolonged disruption of our clinical trials, suppliers or contract manufacturers, extended closures of facilities, such as clinical trial sites, suppliers, manufacturers and distributors, including single source suppliers, and delays with respect to regulatory approvals or the commercialization of any of our products candidates, if approved. Such events may materially and adversely affect our business operations and financial condition. Additionally, the COVID-19 pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could impact our ability to raise additional funds and has also impacted, and may continue to impact, the volatility of our stock price and trading in our stock. Moreover, it is possible the COVID-19 pandemic will significantly impact economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business, our operations or the global and political environment as a whole but it has the potential to materially adversely affect our business, financial condition, results of operations, and prospects.

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 as well as the prior written consent of SVB pursuant to the terms of the Loan and Security Agreement. If we do identify suitable candidates for acquisition, we may not be able to make such acquisitions on favorable terms, or at all, and we may not be able to obtain approval of or consent to such acquisitions from holders of the Securities or SVB. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our ordinary shares or other equity securities to the shareholders of the acquired company, which would reduce the percentage ownership of our then current shareholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Taxation

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

We were a passive foreign investment company (PFIC) for U.S. federal income tax purposes for our taxable year ended December 31, 2017.Based on our gross income and average value of our gross assets, we do not believe we (or our wholly owned non-U.S. 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, 2021; 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".

As used in this section, *Risks Related to Taxation*, the term "U.S. Holder" means a beneficial owner of our ordinary shares (other than a partnership or other pass-through entity) 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.

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. T he 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 holdermay 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, 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 $4.38 on May 19, 2020 and a low price of $0.457 on October 28, 2020 in the twelve-month period ending on March 11, 2021. During this time, the price per ordinary share has ranged from an intra-day low of $0.45 per share to an intra-day high of $6.02 per share. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme

volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their ordinary shares at or above the price paid for the shares. 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 or disapproval of oral sulopenem, sulopenem or future 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;
- 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 by securities analysts;
- announcements by us or our competitors of new product candidates, significant contracts, commercial relationships, acquisitions or capital commitments;
- announcements relating to future development or license agreements including termination of such agreements;
- adverse developments with respect to our intellectual property rights or those of our principal collaborators;
- commencement of litigation involving us or our competitors;
- changes in our board of directors or management;
- new legislation in the United States relating to the prescription, sale, distribution or pricing of drugs;
- product liability claims, other litigation or public concern about the safety of oral sulopenem, sulopenem or future products;
- failure to comply or regain compliance 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;
- 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, like COVID-19; and
- the other factors described in this "Risk Factors" section.

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

If we fail to maintain compliance with the listing requirements of the Nasdaq 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.

On July 15, 2020, we received a letter from the Listing Qualifications Department of The Nasdaq Stock Market LLC (Nasdaq) notifying us that, for the last 30 consecutive business days, the market value of our listed securities was less than the minimum $50,000,000 requirement for inclusion on The Nasdaq Global Market pursuant to Nasdaq Listing Rule 5450(b)(2)(A) (the MVLS Rule). In accordance with Nasdaq Listing Rule 5810(c)(3)(C), we were provided an initial period of 180 calendar days, or until January 11, 2021, to regain compliance with the MVLS Rule.

In December 2020, we applied to transfer the listing of our ordinary shares from The Nasdaq Global Market to The Nasdaq Capital Market. On December 18, 2020, we received a letter from Nasdaq approving our request to transfer the listing of our ordinary shares to The Nasdaq Capital Market. This transfer became effective at the opening of business on December 23, 2020 . Nasdaq indicated that in connection with the transfer to The Nasdaq Capital Market, we regained compliance with the MVLS Rule and the matter was closed.

On September 24, 2020 we received a letter from the Listing Qualifications Department notifying us that we were not in compliance with Nasdaq Listing Rule 5450(b)(2)(C) (the MVPHS Rule) and, in accordance with Nasdaq Listing Rule 5810(c)(3)(D), had an initial period of 180 calendar days, or until March 23, 2021, to regain compliance with the MVPHS Rule. On December 14, 2020, we received notification from Nasdaq that, for 13 consecutive trading days, from November 24, 2020 to December 11, 2020, the market value of our publicly held shares (MVPHS) had been $15.0 million or greater, indicating that we had regained compliance with the MVPHS Rule and the matter was closed.

On September 24, 2020, we received a separate letter from the Listing Qualifications Department, indicating that, based on the closing bid price for the previous 30 consecutive business days, the listing of our ordinary shares was not in compliance with Nasdaq Listing Rule 5450(a)(1) to maintain a minimum bid price of $1.00 per share (the Bid Price Rule). Under Nasdaq Listing Rule 5810(c)(3)(A), we had a period of 180 calendar days, or until March 23, 2021, to regain compliance with the Bid Price Rule. On January 22, 2021, we received formal notification from Nasdaq confirming that for the period from January 7 to January 21, 2021 the closing bid price of our ordinary shares had been $1.00 per share or greater. Accordingly, Nasdaq confirmed that we had regained compliance with the Bid Price Rule and that the matter was closed.

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 deficiencies in the past, there can be no assurance that we will be successful in maintaining the listing of our ordinary shares on the Nasdaq Capital Market or regaining compliance with 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 (i) an event of default under the Loan and Security Agreement, which could lead to an acceleration of amounts due under the Loan and Security Agreement and foreclosure upon and/or sale or other liquidation of all of our and our subsidiaries' assets, including intellectual property; and (ii) a fundamental change under the 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 the Private Placement and 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 equato the Maximum Return for each RLN, less payments made through and including the redemption date, plus certain accrued but unpaid default interest (if any). Upon a change of control of our company, we will require the ultimate beneficial owner or owners controlling the acquiring person or persons to guarantee the obligations of Iterum Bermuda under the RLN Indenture. In the event that a change of control occurs before we receive FDA approval with respect to one or more specified sulopenem products, the redemption price per RLN will be reduced to 50% of the Maximum Return for each RLN, less payments made through and including the redemption date, plus certain accrued but unpaid default interest (if any).

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

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

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

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 February 28, 2021, approximately $16.2 million aggregate principal amount of Exchangeable Notes remained outstanding. The warrants that we issued the purchasers and/or the designees of the placement agent and underwriter, as applicable, in connection with the June 3 Offering, the June 30 Offering, the October 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. Additionally, the exercise of outstanding options and vesting of restricted share units under our equity incentive plans or inducement grants or exercise of other outstanding warrants, including warrants issued to SVB and Life Sciences Fund II LLC, 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 ordinary shares issuable in connection with the exchange of the Exchangeable Notes issued as part of the Private Placement, among other securities, and 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. Also, in connection with our June 3 Offering and June 30 Offering, we filed a registration statement providing for the resale by the purchasers in such offerings of ordinary shares issued and issuable upon exercise of the warrants purchased in such offerings and a substantial portion of the warrants have been exercised. As a result, the shares issuable upon exchange of such notes and upon exercise of such warrants are able to be sold by the holders thereof without restrictions, subject to compliance with securities laws.

Furthermore, ordinary shares that are issuable upon exercise of outstanding options or reserved for future issuance under our equity incentive plans or are issuable upon exercise of our other 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 "emerging growth company," and the reduced disclosure requirements applicable to "emerging growth companies" may make our ordinary shares less attractive to investors.

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

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

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

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of the applicable listing standards of the Nasdaq 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 an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we engaged and continue to engage in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as

documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. Additionally, we will be unable to issue securities in the public markets through the use of a shelf registration if we are not in compliance with Section 404.

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

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

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

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

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

Our Articles 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. The negative covenants in the EN Indenture also prohibit us from undergoing a change of control transaction, other than a transaction in which each Exchangeable Note holder receives cash consideration of at least 300% of the outstanding principal amount of its notes. Furthermore, the EN Indenture prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the Exchangeable Notes, the EN Indenture and the guarantees. In addition, the RLN Indenture prohibits us from engaging in certain mergers or acquisitions unless , among other things, the surviving entity assumes our obligations under the RLNs, the RLN Indenture and the guarantees and the RLN Indenture prohibits us from selling, transferring or assigning

certain assets and prohibits Iterum Bermuda, the Guarantors or any of our significant subsidiaries from undergoing a change of control, other than in connection with a change of control of us. These and other provisions in the EN Indenture and the RLN Indenture could deter or prevent a third party from acquiring us even when the acquisition may be favorable to the holders of our ordinary shares.

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

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

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

Under the Irish Takeover Rules, if an acquisition of ordinary shares were to increase the aggregate holding of the acquirer and its concert parties to ordinary shares that represent 30% or more of the voting rights of the company, 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.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical and biotechnology companies have experienced significant share price volatility in recent years. In addition, we may be subject to securities class action litigation as a result of the financings. If we face any such litigation, we could incur substantial costs defending the lawsuit and the time and attention of our management would be diverted from our business and operations, which could harm our business. We could also be subject to damages claims if we are found to be at fault in connection with a decline in our share price.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our headquarters are located in Dublin, Ireland, where we lease approximately 5,551 square feet of office space. Our lease extends through November 2026, and we have the option to terminate the lease in November 2021 with one year's notice and a six months' rent penalty. We exercised our option to terminate this lease in November 2020.

In June 2018 we entered into a lease for a commercial unit in Dublinthat extends through June 2038, with the option to terminate the lease in June 2028 withno penalty provided one year's notice is given. In September 2020 we entered into a sub-lease agreement for this commercial unit in Dublin that extends through September 2023.

We also lease office space in Old Saybrook, Connecticut. Our lease extends through June 2022, and we have the option to extend the term of the lease for such space through June 2025.

We also lease office space in Chicago, Illinois. Our lease extends through June 2023, and we have the option to extend the term of the lease for such space through June 2028. We believe that our current facilities are adequate to meet our near-term needs, and that suitable additional or substitute space will be available as needed on commercially reasonable terms.

Item 3. Legal Proceedings.

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

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Between May 25, 2018 and December 22, 2020, our ordinary shares have been 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 28, 2021, we had approximately 13 shareholders of record of our ordinary shares. The actual number of shareholders is greater than this number of record holders and includes shareholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

Dividends

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

Recent Sales of Unregistered Securities

From January 1, 2020 through December 31, 2020, we sold and issued the following securities that were not registered under the Securities Act of 1933, as amended (the "Securities Act"):

(1) On January 21, 2020, Iterum Therapeutics Bermuda Limited, our wholly-owned subsidiary ("Iterum Bermuda"), issued, and we and each of our other subsidiaries guaranteed, an aggregate of 51,588 Units consisting of (i) 6.500% Exchangeable Senior Subordinated Notes due 2025 (the "Exchangeable Notes"), issued by Iterum Bermuda in the aggregate original principal amount of $51.6 million, fully and unconditionally guaranteed on an unsecured senior subordinated basis by us and each of our other subsidiaries, and (ii) Limited Recourse Royalty-Linked Subordinated Notes, issued by Iterum Bermuda in the aggregate original principal amount of $0.1 million, fully and unconditionally guaranteed on an unsecured senior subordinated basis by us and each of our other subsidiaries, for an aggregate purchase price of $51.6 million, before deducting placement agent fees and estimated offering expenses. SVB Leerink acted as the exclusive placement agent and received commissions of $1.4 million in connection with the private placement. 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 1,286.1845 shares per $1,000 principal and interest on the Exchangeable Note (equivalent to an exchange price of approximately $0.7775 per ordinary share) as of November 2, 2020, which was adjusted from the initial exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $1.00 per ordinary share), and is subject to further adjustment pursuant to the terms of the indenture governing the Exchangeable Notes. The Exchangeable Notes will mature on January 31, 2025.

(2) On June 3, 2020, we entered into a securities purchase agreement with Intracoastal Capital, LLC, Armistice Capital Master Fund, Ltd., and Lincoln Park Capital Fund, LLC. Pursuant to the securities purchase agreement, we issued to such investors warrants to purchase up to 1,485,885 ordinary shares. The warrants have an exercise price of $1.62 per share, are immediately exercisable and expire on December 5, 2025. H. C. Wainwright & Co., LLC ("Wainwright") acted as placement agent for the offering and received commissions of $350,000 in connection with the offering. As consideration for the services provided to us by Wainwright as placement agent for the offering, we issued placement agent warrants to purchase an aggregate of 208,023 ordinary shares to designees of Wainwright. The placement agent warrants have an exercise price of $2.1031 per share, are immediately exercisable and expire on June 3, 2025.

(3) On June 30, 2020, we entered into a securities purchase agreement with Intracoastal Capital, LLC, Armistice Capital Master Fund, Ltd., and Anson Investments Master Fund LP. Pursuant to the securities purchase agreement, we issued to such investors warrants to purchase up to 1,686,343 ordinary shares. The warrants have an exercise price of $1.42 per share, are immediately exercisable and expire on January 2, 2026. Wainwright acted as placement agent for the offering and received commissions of $350,000 in connection with the offering. As partial consideration for the services provided to us by Wainwright as placement

agent for the offering, we issued placement agent warrants to purchase an aggregate of 236,088 ordinary shares to designees of Wainwright. The placement agent warrants have an exercise price of $1.8531 per share, are immediately exercisable and expire on June 30, 2025.

The offer, sale and issuance of the securities in the private placement transactions described in paragraphs 1, 2 and 3 above were exempt from registration under Section 4(a)(2) of the Securities Act (or Regulation D promulgated thereunder) in that the transactions were by an issuer not involving any public offering and appropriate legends were placed upon the securities issued in these transactions. The sale of these securities were made without any general solicitation or advertising.

Use of Proceeds from Registered Securities

Not applicable.

Purchases of Equity Securities by the Issuer

None.

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

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

Overview

We are a 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 successfully 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 all 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 superiority to ciprofloxacin, providing evidence of a treatment effect in patients with uUTI. Based on discussions with the FDA at a pre-New Drug Application, or 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. The FDA has designated our application as a priority review and consequently assigned a PDUFA (Prescription Drug User Fee Act) goal date for completion of the review of oral sulopenem of July 25, 2021. The FDA currently plans to hold an advisory committee meeting on June 2, 2021 to discuss the NDA.

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

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

and at prices and on terms that we may determine.As of February 28, 2021, we had issued $98.1 million of securities registered under our universal shelf registration statement.

On January 21, 2020, we completed a private placement (Private Placement) pursuant to which our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), issued and sold approximately $51.6 million aggregate principal amount of 6.500% Exchangeable Senior Subordinated Notes due 2025 (Exchangeable Notes) and $0.1 million aggregate principal amount of Limited Recourse Royalty-Linked Subordinated Notes (RLNs and, together with the Exchangeable Notes, the Securities) to a group of accredited investors. On September 8, 2020, we completed a rights offering (the Rights Offering) pursuant to which our wholly owned subsidiary, Iterum Bermuda, issued and sold approximately $0.2 million aggregate principal amount of Exchangeable Notes and $0.02 million aggregate principal amount of RLNs to existing shareholders. The Securities were sold in units (the Units), with each Unit consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs. The Units were sold at a price of $1,000 per Unit. As of January 21, 2021, subject to specified limitations, the Exchangeable Notes are exchangeable for our ordinary shares at an exchange rate of 1,286.1845 shares per $1,000 principal and interest on the Exchangeable Note (equivalent to an exchange price of approximately $0.7775 per ordinary share) as of November 2, 2020, which was adjusted from the initial exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $1.00 per ordinary share) and is subject to further adjustment pursuant to the terms of the indenture governing the Exchangeable Notes. 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. Pursuant to the indenture governing the RLNs, the payments on the RLNs will be up to either 15% or 20% of net revenues from U.S. sales of such products, depending on the indication approved by the FDA. The aggregate amount of payments on each RLN is capped at $160.00 (or 4,000 times the principal amount of such RLN). Iterum Bermuda received net proceeds from the sale of the Securities in the Private Placement and the Right Offering of approximately $45.0 million, after deducting placement agent fees and offering expenses. As of February 28, 2021, approximately $16.2 million aggregate principal amount of Exchangeable Notes remained outstanding.

In April 2020, we began deferring payment on our share of U.S. payroll taxes owed, as allowed by the Coronavirus Aid Relief and Economic Security Act (CARES Act) through December 31, 2020. We are able to defer half of our share of U.S. payroll taxes owed until December 31, 2021, with the remaining half due on December 31, 2022.

On April 3, 2020, the U.S. Small Business Administration (SBA) launched a Paycheck Protection Program (the 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 a note (PPP loan) with Silicon Valley Bank (SVB) (the Lender) under the Program, pursuant to the Borrower receiving a PPP 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 by us 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 will be 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 of $26 through March 2022.

On June 3, 2020, we entered into a Securities Purchase Agreement (June 3 SPA) with certain institutional investors (the June 3 Purchasers) pursuant to which we issued and sold, in a registered direct offering (the June 3 Offering), an aggregate of 2,971,770 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $1.6825, 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 Offering pursuant to our universal shelf registration statement on Form S-3. Pursuant to the June 3 SPA, in a concurrent private placement, we issued and sold to the June 3 Purchasers warrants to purchase up to 1,485,885 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $1.62 per ordinary share, subject to adjustment in certain circumstances, and will expire on December 5, 2025. The closing date of the June 3 Offering was June 5, 2020. Warrants to purchase 208,023 ordinary shares, amounting to 7% of the ordinary shares issued under the June 3 SPA, were issued to designees of the placement agent on closing of the June 3 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $2.1031 per ordinary share, and will expire on June 3, 2025.

On June 30, 2020, we entered into a securities purchase agreement (June 30 SPA) with certain institutional investors (the June 30 Purchasers) pursuant to which we issued and sold in a registered direct offering (the June 30 Offering) an aggregate of 3,372,686 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $1.4825, 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 Offering pursuant to our universal shelf registration statement on Form S-3. Pursuant to the June 30 SPA, in a concurrent private placement, we issued and sold to the June 30 Purchasers warrants to purchase up to 1,686,343 ordinary shares. Upon closing the warrants were exercisable immediately at an exercise price of $1.42 per ordinary share, subject to adjustment in certain circumstances, and will expire on January 2, 2026. The June 30 Offering closed on July 2, 2020. Warrants to purchase 236,088 ordinary shares, amounting to 7% of the ordinary shares issued under the June 30 SPA, were issued to

designees of the placement agent on closing of the June 30 Offering. Upon closing, the warrants issued to such designeesbecame exercisable immediately at an exercise price of $1.8531 per ordinary share, and will expire on June 30, 2025.

On October 27, 2020, we completed a registered public offering (the October Offering) in which we sold an aggregate of (i) 15,511,537 ordinary shares, $0.01 nominal value per share, (ii) pre-funded warrants exercisable for an aggregate of 11,411,539 ordinary shares and (iii) warrants exercisable for an aggregate of 20,192,307 ordinary shares. The pre-funded warrants were issued and sold to certain purchasers whose purchase of ordinary shares in the October 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 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 $0.65 per ordinary share and warrant and $0.64 per pre-funded warrant and warrant. Our net proceeds from the October 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 $0.65 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 $0.01 per ordinary share, subject to adjustment in certain circumstances, and expire when exercised in full, subject to certain conditions. As of December 31, 2020, all pre-funded warrants had been exercised for net proceeds of $0.11 million. In connection with the October Offering, we entered into a Securities Purchase Agreement (the 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 and ongoing covenants of ours, including a prohibition on issuance of ordinary shares or securities convertible or exchangeable into ordinary shares by us for a period of 45 days after the closing of the October Offering and a prohibition on us entering into variable rate transactions for a period of 12 months after the closing of the October Offering, subject to certain exceptions. Warrants to purchase 1,884,615 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 Offering, were issued to designees of the placement agent on closing of the October Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $0.8125 per ordinary share and expire on October 22, 2025.

On February 3, 2021, we entered into an amended and restated underwriting agreement (the Underwriting Agreement) withH. C. Wainwright & Co., LLC as the sole underwriter to issue and sell 34,782,609 ordinary shares, $0.01 nominal value per share, in an underwritten public offering with a public offering price of $1.15 per share (the February Underwritten Offering). We offered the ordinary shares in the February Underwritten Offering pursuant to our universal shelf registration statement on Form S-3. The February 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 5,217,391 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 Underwritten Offering to 40,000,000 shares, which resulted in aggregate net proceeds to us of approximately $42.1 million after deducting underwriting discounts and commissions and estimated offering expenses. In addition, pursuant to the Underwriting Agreement, we issued upon the closing of the February Underwritten Offering to the underwriter's designees warrants to purchase 2,800,000 ordinary shares, amounting to 7.0% of the aggregate number of ordinary shares sold in the February Underwritten Offering. The warrants issued to such designees of the underwriter have an exercise price of $1.4375 per ordinary share, were exercisable upon issuance and will expire on February 3, 2026.

On February 9, 2021, we entered into a securities purchase agreement (the February SPA) with several healthcare-focused institutional investors pursuant to which we agreed to issue and sell in a registered direct offering (the February Registered Direct Offering) an aggregate of 17,500,000 ordinary shares, $0.01 nominal value per share, at a purchase price of $2.00 per share, for aggregate net proceeds to us of approximately $32.2 million after deducting placement agent fees and other estimated offering expenses. We offered the ordinary shares in the February Registered Direct Offering pursuant to our universal shelf registration statement on Form S-3. The February Registered Direct Offering closed on February 12, 2021. Warrants to purchase 1,225,000 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 Registered Direct Offering. Upon closing, warrants issued to such designees became exercisable immediately at an exercise price of $2.50 per ordinary share, subject to adjustment in certain circumstances, and will expire on February 9, 2026.

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, 2020, we had an accumulated deficit of $286.9 million. We expect to continue to incur significant expenses for the foreseeable future as we seek regulatory approval and engage in market preparation and pre-commercialization activities. 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. We are currently evaluating our commercialization strategy in the United States; however, we expect to work with a third-party provider of commercialization services to launch oral sulopenem and have engaged a leading provider of commercial services to the life science industry to initiate pre-launch activities for oral sulopenem, followed by

planned commercialization services upon final agreement. We may also incur expenses in connection with the clinical development of sulopenem in additional indications, the establishment of additional sources for the manufacture of sulopenem tablets and IV vials or the in-license or acquisition of additional product candidates. Additionally, we have incurred and expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

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

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

As of December 31, 2020, we had cash, cash equivalents and restricted cash of $14.8 million. We believe that our existing cash and cash equivalents, together with the aggregate net proceeds of $74.3 million from the February Underwritten Offering and from the February Registered Direct Offering, and proceeds received from the exercise of warrants subsequent to December 31, 2020, should be sufficient to fund our operating expenses and capital expenditure requirements into the first half of 2023, including through the PDUFA goal date of July 25, 2021 for completion of the FDA's review of the NDA for oral sulopenem and the potential commercial launch of oral sulopenem, if approved. However, this estimate is based on assumptions that may prove to be wrong, and our operating plans may change as a result of many factors and various risks and uncertainties.

We are currently evaluating our corporate, strategic, financial and financing alternatives, with the goal of maximizing value for our stakeholders. These alternatives could potentially include the licensing, sale or divestiture of our assets or proprietary technologies, a sale of our company, a merger or other business combination or another strategic transaction involving us. 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.

COVID-19 Global Pandemic

In December 2019, an outbreak of COVID-19 was reported in Wuhan, China. On March 11, 2020, the World Health Organization declared COVID-19 a global pandemic and on March 13, 2020, President Donald J. Trump declared the virus a national emergency. This highly contagious disease has spread to most of the countries in the world and throughout the United States, creating a serious impact on customers, workforces, and suppliers, disrupting economies and financial markets, and potentially leading to a world-wide economic downturn. It has caused a disruption of the normal operations of many businesses, including the temporary closure or scale-back of business operations and/or the imposition of either quarantine or remote work or meeting requirements for employees, either by government order or on a voluntary basis. The pandemic may impact the ability of our strategic partners to operate and fulfill their contractual obligations, and result in an increase in their costs and cause delays in performance. These effects, and the direct effect of the virus and any potential disruption on our operations, may negatively impact our ability to meet our strategic targets. Our employees, in most cases, are working remotely due to safety concerns and using various technologies to perform their functions. We feel we have sufficient office and IT resources to allow employees to return to office work or work from home indefinitely based on the latest government advice. Additionally, the disruption and volatility in the global and domestic capital markets may increase the cost of capital and limit our ability to access capital. Both the health and economic aspects of COVID-19 are highly fluid and the future course of each is uncertain. For these reasons and other reasons that may come to light if the coronavirus pandemic and associated protective or preventative measures expand, we may experience a material adverse effect on our business operations and financial condition; however, its ultimate impact is highly uncertain and subject to change.

We cannot foresee if and when the outbreak of COVID-19 will be effectively contained, nor can we predict the severity and duration of its impact. Covid-19 has not yet had a significant impact on the Company's day to day operations. Management is actively monitoring the global situation on our financial condition, liquidity, operations, suppliers, industry, and workforce. Given the daily evolution of the COVID-19 outbreak and the global responses to curb its spread, we are not able to estimate the adverse effects of the COVID-19 outbreak on our results of operations, financial condition, or liquidity.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of oral sulopenem or sulopenem in the near future . If our development efforts for our sulopenem program are successful and result in regulatory approval and/or license agreements with third parties, we may generate revenue in the future from product sales. To date, all of our revenue has been derived from our Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, award. We expect that our revenue for the foreseeable future will be derived primarily from payments under government awards that we may enter into in the future. In June 2017, CARB-X awarded us funds of up to $1.5 million to advance the development of our sulopenem program. The CARB-X award was structured as a cost reimbursement arrangement and was recognized over a period of 20 months from August 2017 to March 2019.

Operating Expenses

Research and Development Expenses

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

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

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

Research and development activities are central to our business model. Product candidates in advanced stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later stage clinical trials. As a result, our research and development expenses increased substantially throughout 2019 as we substantially completed the Phase 3 clinical trials for our sulopenem program, increased personnel costs, including share-based compensation, conducted other clinical trials and prepared for regulatory filings for oral sulopenem and sulopenem.

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

- the impact of the COVID-19 pandemic on the economy and our business generally including timing of regulatory review, potential approval and commercialization of any future products, including sulopenem for the treatment of uUTI;
- 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 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; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our clinical trials. 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 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 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. The FDA has designated our application as a priority review and consequently assigned a PDUFA (Prescription Drug User Fee Act) goal date for completion of the review of oral sulopenem of July 25, 2021. The FDA currently plans to hold an advisory committee meeting on June 2, 2021 to discuss the 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.

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 and market preparation expenses.

If and when we believe regulatory approval of oral sulopenem and/or sulopenem appears likely, we anticipate an increase in payroll and expenses as a result of our preparation for commercial operations.

Interest Expense, Net

Interest expense, net consists of interest incurred and amortization of debt costs on our loan from SVB, interest incurred on our PPP loan, interest accrued and amortization of debt costs with respect to the Exchangeable Notes and RLNs and interest earned on our cash and cash equivalents, which are generally invested in money market accounts. 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 at which time any accrued and unpaid interest becomes due and payable.

Financing Transaction Costs

Financing transaction costs consist of the portion of transaction costs incurred in relation to the Private Placement and the Rights Offering allocated to derivative liabilities (the Derivative liability).

Adjustments to Fair Value of Derivatives

Derivative liabilities are revalued at each balance sheet date and the change in fair value during the reporting period is recorded in other income, net in the consolidated statements of operations as adjustments to the fair value of derivatives.

Other Income, Net

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

Provision for Income Taxes

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

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

Critical Accounting Policies and Significant Judgments and Estimates

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

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

Accrued Research and Development Expenses

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

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

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

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

Share-Based Compensation

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

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

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

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

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

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

We have elected to account for forfeitures as they occur.

Determination of the Fair Value of Ordinary Shares prior to IPO

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

- the prices at which we sold preferred shares and the superior rights and preferences of the preferred shares relative to our ordinary shares at the time of each grant;
- the progress of our research and development programs, including the status of preclinical studies and clinical trials for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the pharmaceutical industry and trends within the pharmaceutical industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our ordinary shares and our preferred shares;

- the likelihood of achieving a liquidity event, such as an initial public offering or a sale of our company in light of prevailing market conditions; and
- the analysis of initial public offerings and the market performance of similar companies in the pharmaceutical and biotechnology industries.

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

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

Derivative Liability

We account for derivative instruments in accordance with 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 other (expense) / income, net.

In determining the appropriate fair values, we use a variety of valuation techniques applying DCF, Black-Scholes and binomial lattice models. 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.

Royalty-Linked Notes

The RLNs qualify as debt instruments under ASC 470, *Debt*, and are initially recorded at fair value, applying a DCF model, and then subsequently measured at amortized cost. We assess the valuation of this debt for any significant changes to the facts and circumstances in the initial valuation which would impact the carrying value, and if required, make adjustments to revalue the debt as appropriate. Amortization is recognized as interest expense over the term of the debt instrument using the effective interest method.

Results of Operations

Comparison of the Years Ended December 31, 2020 and 2019

The following table summarizes our loss before income tax for the years ended December 31, 2020 and 2019:

	Year ended December 31,		
	2020	2019	Change
	(In thousands)		
Revenue	$ —	$ 37	$ (37)
Operating expenses:			
Research and development	21,074	90,774	(69,700)
General and administrative	11,052	11,284	(232)
Total operating expenses	$ 32,126	$ 102,058	$ (69,932)
Operating loss	$ (32,126)	$ (102,021)	69,895
Total other expense	(19,137)	(665)	(18,472)
Loss before income taxes	$ (51,263)	$ (102,686)	$ 51,423

Revenue

In June 2017, CARB-X awarded us funds of up to $1.5 million to advance the development of our sulopenem program. The funds were receivable as we incurred qualifying expenses over a 20-month period from August 2017 to March 31, 2019. During the year ended December 31, 2019, we recognized $0.0 million of revenue under this award.

Research and Development Expenses

	Year ended December 31,		
	2020	2019	Change
	(In thousands)		
CRO and other preclinical and clinical trial expenses	$ 9,881	$ 71,962	$ (62,081)
Personnel related (including share-based compensation)	3,031	7,971	(4,940)
Chemistry, manufacturing and control (CMC) related expenses	4,682	7,560	(2,878)
Consulting fees	3,480	3,281	199
Total research and development expenses	$ 21,074	$ 90,774	$ (69,700)

The decrease in CRO and other preclinical and clinical trial expenses of $62.1 million was primarily due to a decrease in costs incurred related to our three Phase 3 clinical trials, which completed enrollment in the second half of 2019. Personnel related expenses decreased by $4.9 million as a result of a reduction in headcount in our CMC and clinical functions. Personnel related expenses for the years ended December 31, 2020 and 2019 included share-based compensation expense of $0.8 million and $0.7 million, respectively. CMC related expenses decreased by $2.9 million primarily as a result of the completion of process validation for the active pharmaceutical ingredient by our primary supplier in 2019. The increase in consulting fees of $0.2 million was primarily due to an increase in consultants used for preparation of our NDA filing in the fourth quarter of 2020 partially offset by a decrease in consultants used in relation to our Phase 3 clinical trials.

General and Administrative Expenses

	Year ended December 31,		
	2020	2019	Change
	(In thousands)		
Personnel related (including share-based compensation)	$ 5,433	$ 4,861	$ 572
Facility related and other	3,141	3,308	(167)
Professional and consultant fees	2,478	3,115	(637)
Total general and administrative expenses	$ 11,052	$ 11,284	$ (232)

Personnel related expenses increased by $0.6 million primarily as a result of an increase in share-based compensation for employees in our general and administrative and commercial functions partially offset by a decrease in headcount. Personnel related expenses for the years ended December 31, 2020 and 2019 included share-based compensation expense of $1.8 million and $1.0 million, respectively. Facility related and other costs decreased by $0.2 million primarily as a result of a decrease in directors' fees, Board travel and directors' share-based compensation, partially offset by an increase in insurance. Facility related and other costs for the years ended December 31, 2020 and 2019 included directors' share-based compensation expense of $0.2 million and $0.5 million, respectively. Professional and consulting fees decreased by $0.6 million primarily as a result of a decrease in consultants used for pre-commercialization activities partially offset by increased legal fees.

The following table summarizes our total other expense for the years ended December 31, 2020 and 2019:

	Year ended December 31,		
	2020	2019	Change
	(In thousands)		
Interest expense, net	$ (15,097)	$ (861)	$ (14,236)
Financing transaction costs	(2,848)	—	(2,848)
Adjustments to fair value of derivatives	(1,745)	—	(1,745)
Extinguishment of debt	340	—	340
Other income, net	213	196	17
Total other expense	$ (19,137)	$ (665)	$ (18,472)

Interest Expense, Net

Interest expense, net increased by $14.2 million for the year ended December 31, 2020 primarily as a result of the recognition of $3.2 million of interest expense related to the interest accruing on our Exchangeable Notes and $10.5 million related to amortization of the debt discounts and deferred financing costs relating to the Exchangeable Notes and RLNs, as well as a reduction in interest income of $0.8 million, partially offset by a reduction in interest expense of $0.3 million associated with our credit facility with SVB as principal amortization began in the fourth quarter of 2019 and our interest rate was lower during 2020.

Financing Transaction Costs

Financing transaction costs allocated to the Derivative Liability were $2.8 million for the year ended December 31, 2020. No such expenses were incurred for the year ended December 31, 2019.

Adjustments to Fair Value of Derivatives

Adjustments to the fair value of the Derivative Liability were $1.7 million for the year ended December 31, 2020. No derivative liabilities were recorded for the year ended December 31, 2019.

Extinguishment of Debt

The SBA forgave $0.3 million of the $0.7 million loan we received in 2020 as part of the CARES Act.

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. In addition, in 2020, other income, net also includes sub-lease income of $0.1 million from a sub-lease agreement for a commercial unit.

Comparison of the Years Ended December 31, 2019 and 2018

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

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

Revenue

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

Research and Development Expenses

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

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

General and Administrative Expenses

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

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

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses and negative cash flows from our operations. We have generated limited revenue to date from a funding arrangement with CARB-X. We have funded our operations to date primarily through the issuance of ordinary and convertible preferred shares, 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 and the Rights Offering pursuant to which our wholly owned subsidiary, Iterum Bermuda issued and sold approximately $51.8 million aggregate principal amount of 6.500% Exchangeable Notes and $0.1 million aggregate principal amount of RLNs. Through December 31, 2020, 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 approximately $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 June 3 Offering and the June 30 Offering, net proceeds of $15.5 million from the October Offering and $0.9 million from the exercise of warrants issued in the October Offering.

In connection with the February Underwritten Offering, we receivedaggregate gross proceeds of approximately $46.0 million and net proceeds of approximately $42.1 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. In connection with the February Registered Direct Offering, we received aggregate gross proceeds of approximately $35.0 million and net proceeds of approximately $32.2 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

As of December 31, 2020, we had cash, cash equivalents and restricted cash of $14.8 million.

Secured credit facility

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

Required monthly amortization payments for the initial $15.0 million draw commenced on November 1, 2019 and total principal repayments of $6.2 million were made during the year ended December 31, 2020. Interest accrues at a floating per annum rate equal to the greater of (i) 8.31%; or (ii) 3.89% above the Wall Street Journal prime rate, and is payable monthly in arrears. All outstanding principal, plus a 4.20% final interest payment, will be due and payable on the earliest to occur of March 1, 2022 (the maturity date), the acceleration of the term loan or the prepayment of the term loan. The final payment fee of $0.6 million, which represents 4.2% of the funded loan, is accreted using the effective interest method over the life of the loan as interest expense. Voluntary prepayments are permitted at any time, subject to a prepayment fee of 4.00% in the first year, 3.00% in the second year, and 2.00% thereafter.

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

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

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

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 approximately $51.6 million aggregate principal amount of 6.500% 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 our wholly owned subsidiary, Iterum Bermuda, issued and sold approximately $0.2 million aggregate principal amount of 6.500% Exchangeable Notes and $0.02 million 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 our ordinary shares, cash or a combination of ordinary shares and cash, at an exchange rate of 1,286.1845 shares per $1,000 principal and interest on the Exchangeable Note (equivalent to an exchange price of approximately $0.7775 per ordinary share) as of November 2, 2020, which was adjusted from the initial exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $1.00 per ordinary share) and is subject to further adjustment pursuant to the terms of the indenture governing the Exchangeable Notes. The Exchangeable Notes will mature on January 31, 2025. As of February 28, 2021, approximately $16.2 million aggregate principal amount of Exchangeable Notes remained outstanding. 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. Pursuant to the indenture governing the RLNs, the payments on the RLNs will be up to either 15% or 20% of net revenues from U.S. sales of such products, depending on the indication approved by the FDA. The aggregate amount of payments on each RLN is capped at $160.00 (or 4,000 times the principal amount of such RLN). Iterum Bermuda received net proceeds from the sale of the Units in the Private Placement and the Rights Offering of approximately $45.0 million, after deducting placement agent fees and offering expenses.

Registered Direct Offerings

On June 3, 2020, we entered into the June 3 SPA with the June 3 Purchasers pursuant to which we issued and sold, in the June 3 Offering, an aggregate of 2,971,770 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $1.6825, 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 Offering pursuant to our universal shelf registration statement on Form S-3. Pursuant to the June 3 SPA, in a concurrent private placement, we issued and sold to the June 3 Purchasers warrants to purchase up to 1,485,885 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $1.62 per ordinary share, subject to adjustment in certain circumstances, and will expire on December 5, 2025. The closing date of the June 3 Offering was June 5, 2020. Warrants to purchase 208,023 ordinary shares, amounting to 7% of the ordinary shares issued under the June 3 SPA, were issued to designees of the placement agent on the closing of the June 3 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $2.1031 per ordinary share, and will expire on June 3, 2025.

On June 30, 2020, we entered into the June 30 SPA with the June 30 Purchasers pursuant to which we issued and sold in the June 30 Offering an aggregate of 3,372,686 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $1.4825, 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 Offering pursuant to our universal shelf registration statement on Form S-3. Pursuant to the June 30 SPA, in a concurrent private placement, we issued and sold to the June 30 Purchasers warrants to purchase up to 1,686,343 ordinary shares. Upon closing, the warrants were exercisable immediately at an exercise price of $1.42 per ordinary share, subject to adjustment in certain circumstances, and will expire on January 2, 2026. The June 30 Offering closed on July 2, 2020. Warrants to purchase 236,088 ordinary shares, amounting to 7% of the ordinary shares issued under the June 30 SPA, were issued to designees of the placement agent on closing of the June 30 Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $1.8531 per ordinary share, and will expire on June 30, 2025.

On February 9, 2021, we entered into the February SPA pursuant to which we issued and sold in the February Registered Direct Offering an aggregate of 17,500,000 ordinary shares, $0.01 nominal value per share, at a purchase price of $2.00 per share, for aggregate net proceeds to us of approximately $32.2 million after deducting placement agent fees and other estimated offering expenses payable by us. We offered the ordinary shares in the February Registered Direct Offering pursuant to our universal shelf registration statement on Form S-3. The February Registered Direct Offering closed on February 12, 2021. Warrants to purchase 1,225,000 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 Registered Direct Offering. Upon closing, warrants issued to such designees became exercisable immediately at an exercise price of $2.50 per ordinary share, subject to adjustment in certain circumstances, and will expire on February 9, 2026.

October Offering

On October 27, 2020, we completed the October Offering in which we sold an aggregate of (i) 15,511,537 ordinary shares, $0.01 nominal value per share, (ii) pre-funded warrants exercisable for an aggregate of 11,411,539 ordinary shares and (iii) warrants exercisable for an aggregate of 20,192,307 ordinary shares. The pre-funded warrants were issued and sold to certain purchasers whose purchase of ordinary shares in the October 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 the Company's outstanding ordinary shares immediately following the consummation of the October 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 $0.65 per ordinary share and warrant and $0.64 per pre-funded warrant and warrant. Our net proceeds from the October 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 $0.65 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 $0.01 per ordinary share, subject to adjustment in certain circumstances, and expire when exercised in full, subject to certain conditions. As of December 31, 2020, all pre-funded warrants had been exercised for net proceeds of $0.11 million. In connection with the October 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 and ongoing covenants of ours, including a prohibition on issuance of ordinary shares or securities convertible or exchangeable into ordinary shares by us for a period of 45 days after the closing of the October Offering and a prohibition on us entering into variable rate transactions for a period of 12 months after the closing of the October Offering, subject to certain exceptions. Warrants to purchase 1,884,615 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 Offering, were issued to designees of the placement agent on closing of the October Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $0.8125 per ordinary share and expire on October 22, 2025.

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 are able to defer half of our share of U.S. payroll taxes owed until December 31, 2021, with the remaining half due on December 31, 2022.

On April 3, 2020 the SBA launched the Program, which was established following the signing of the CARES Act on March 27, 2020. On April 30, 2020, our wholly owned subsidiary, the Borrower, entered into the PPP loan with the Lender under the 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 SBA remits the forgiveness amount to the Borrower or until after the Deferral Period. Following the Deferral Period, equal monthly repayments of principal and interest will be 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, and the remaining loan of $0.4 million began amortization in December with equal monthly repayments through March 2022.

February 2021 Underwritten Offering

On February 3, 2021, we entered into an Underwriting Agreement pursuant to which we issued and sold the February Underwritten Offering 34,782,609 ordinary shares, $0.01 nominal value per share, at a public offering price of $1.15 per share. We offered the ordinary shares in the February Underwritten Offering pursuant to our universal shelf registration statement on Form S-3. The February 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 5,217,391 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 Underwritten Offering to 40,000,000 shares, which resulted in aggregate net proceeds of approximately $42.1 million after deducting underwriting discounts and commissions and estimated offering expenses. In addition, pursuant to the Underwriting Agreement, we agreed to issue to the underwriter's designees warrants to purchase 2,800,000 ordinary shares, which is equal to 7.0% of the aggregate number of ordinary shares sold in the February Underwritten Offering. The warrants issued to such designees of the underwriter have an exercise price of $1.4375 per ordinary share, were exercisable upon issuance and will expire on February 3, 2026.

Cash Flows

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

	Year ended December 31,		
	2020	2019	2018
	(In thousands)		
Net cash used in operating activities	$(54,528)	$(81,922)	$(77,252)
Net cash (used in) / provided by investing activities	(11)	40,101	(8,658)
Net cash provided by financing activities	64,475	2,063	122,204
Effect of exchange rates on cash and cash equivalents	(11)	(22)	(108)
Net increase / (decrease) in cash	$9,925	$(39,780)	$36,186

Operating Activities

During the year ended December 31, 2020, operating activities used $54.5 million of cash, resulting from our net loss of $52.0 million and net cash used by changes in our operating assets and liabilities of $24.5 million, partially offset by non-cash charges of $19.2 million and financing transaction costs reclassified to financing activities of $2.8 million. Net cash used by changes in our operating assets and liabilities for the year ended December 31, 2020 consisted primarily of decreases in accounts payable and accrued expenses, primarily due to payments made for clinical trial expenses incurred in the fourth quarter of 2019 and lower clinical trial expenses for the year ended December 31, 2020.

During the year ended December 31, 2019, operating activities used $81.9 million of cash, resulting from our net loss of $103.1 million, partially offset by net cash provided by changes in our operating assets and liabilities of $17.9 million and non-cash charges of $3.3 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2019 consisted primarily of increases in accounts payable and accrued expenses, primarily due to increases in clinical trial expenses, and a decrease in prepaid expenses and other current assets, largely related to the use of prepayments previously made to contract research organizations, partially offset by an increase in other assets, primarily related to advance payments to a supplier for equipment, and a decrease in other liabilities as a result of payments made for operating leases.

During the year ended December 31, 2018, operating activities used $77.3 million of cash, resulting from our net loss of $77.1 million and net cash used by changes in our operating assets and liabilities of $1.6 million, partially offset by non-cash charges of $1.3 million. Net cash used by changes in our operating assets and liabilities for the year ended December 31, 2018 consisted primarily of increases in prepaid expenses and other current assets, largely related to advance payments to contract research organizations, and other assets, largely related to a deposit paid for the Dublin commercial lease and advance payments to CMOs, partially offset by increases in accounts payable and accrued expenses, primarily due to an increase in clinical trial expenses.

Investing Activities

During the year ended December 31, 2020, net cash used in investing activities was related to purchases of property and equipment. During the year ended December 31, 2019, net cash provided by investing activities of $40.1 million was primarily related to sales of short-term investments. During the year ended December 31, 2018, net cash used in investing activities of $8.7 million was related to purchases of short-term investments of $96.5 million and purchases of property and equipment of $0.1 million, partially offset by sales of short-term investments of $87.9 million.

Financing Activities

During the year ended December 31, 2020, net cash provided by financing activities was $64.5 million and consisted of net cash proceeds of approximately $45.0 million from the Private Placement and the Rights Offering, net cash proceeds of $8.6 million from the June 3 and June 30 Offerings, net cash proceeds of approximately $15.5 million from the October Offering, net cash proceeds of $0.9 million from the exercise of warrants and $0.7 million from the drawdown of the PPP loan, partially offset by principal repayments of $6.2 million made to SVB under the Loan Agreement. During the year ended December 31, 2019, net cash provided by financing activities was $2.1 million and consisted of net cash proceeds from the issuance of ordinary shares under the subscription agreement with a supplier of $3.1 million, partially offset by principal repayments of $1.0 million made to SVB under the Loan Agreement. During the year ended December 31, 2018, net cash provided by financing activities was $122.2 million and consisted of net cash proceeds from the issuance of Series B-2 preferred shares in February 2018 (which converted to ordinary shares in connection with our IPO) of $32.2 million, net cash proceeds from the issuance of ordinary shares in May and June 2018 associated with our IPO of $74.2 million, net cash proceeds from the issuance of ordinary shares under the subscription agreement with a supplier of $1.4 million and net cash proceeds from the SVB loan drawdown of $14.4 million.

Funding Requirements

We expect to continue to incur significant expenses and increasing operating losses as we seek marketing approval for oral sulopenem, carry out 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:

- conduct additional clinical trials for oral sulopenem and/or sulopenem, which include our planned Phase 1 clinical trials related to pediatric indications;
- initiate other studies as part of our sulopenem program, some of which may be required for regulatory approval of our product candidates;
- establish 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 of regulatory review and potential approval of our pending NDA for oral sulopenem for the treatment of uUTI in patients with a quinolone non-susceptible pathogen;
- the timing and costs of clinical trials of our oral sulopenem and sulopenem,including our planned Phase 1 clinical trials related to pediatric indications and any other studies which may be required for regulatory approval of our product candidates;
- the initiation, progress, timing, costs and results of preclinical studies and clinical trials of other potential product candidates and of our current product candidates in additional indications;
- the amount of funding that we receive under government awards that we have applied for or may apply for in the future;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for oral sulopenem and/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 are obligated to make in connection with the RLNs;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property related claims;
- the costs of operating as a public company;

- the extent to which we in-license or acquire other products and technologies;
- the impact of the COVID-19 pandemic on the economy and our business generally, including the impact the pandemic may have on timing of regulatory approval and commercialization of any future products; 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 the COVID-19 pandemic may increase the cost of capital and limit our ability to access capital. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our shareholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our ordinary shareholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our secured credit facility with SVB, 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. The Purchase Agreement entered into in connection with the October Offering and the Underwriting Agreement and February SPA entered into in February 2021 also contain ongoing covenants for us, including a prohibition on issuance of ordinary shares or securities convertible or exchangeable into our ordinary shares for a period of 60 days after the closing of the relevant transaction and a prohibition on us entering into variable rate transactions for a period of 12 months after the closing of the relevant transaction, subject to certain exceptions. 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.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2020, and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments Due by Period				
	Total	Less than 1 year	1 to 3 years	4 to 5 years	More than 5 years
	(In thousands)				
Operating lease commitments (1)	$ 3,499	$ 962	$ 1,135	$ 673	$ 729
Principal loan repayments (2)	60,049	6,516	1,621	51,808	104
Total	$ 63,548	$ 7,478	$ 2,756	$ 52,481	$ 833

(1) See Note 6 to the consolidated financial statements for further details regarding leases.
(2) See Note 8 to the consolidated financial statements for further details regarding debt. Principal payments relate to our SVB loan, our PPP loan, our Exchangeable Notes and our RLNs.

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

Under the indenture governing the RLNs, 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 the Payment Measuring Period ending June 30, 2020 and December 31, 2020. 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). Other than the principal amount of $104, we have not included any payment obligations on the RLNs in the table above as the amount, timing and likelihood of such payments are not known.

Emerging Growth Company Status

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

Off-Balance Sheet Arrangements

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

We had cash, cash equivalents and marketable securities of $14.5 million as of December 31, 2020, consisting primarily of cash and investments in money market funds.

Based on the $7.8 million outstanding under the credit facility as of December 31, 2020, a 100 basis point change in interest rates would have had a $0.04 million impact on our net interest expense in fiscal year 2020. The interest rate on our secured credit facility is sensitive to changes in interest rates. Interest accrues on borrowings under the credit facility at a per annum rate equal to the greater of (i) 8.31%; or (ii) 3.89% above The Wall Street Journal prime rate. The Wall Street Journal prime rate decreased from 5.50% to 5.25% on August 1, 2019, to 5.00% on September 19, 2019, to 4.75% on October 31, 2019, to 4.25% on March 4, 2020 and to 3.25% on March 16, 2020. We do not currently engage in any hedging activities against changes in interest rates.

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, 2020 and 2019, 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, 2020 and 2019. 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, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, convertible preferred shares and shareholders' (deficit)/equity, and cash flows for each of the years in the three-year period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

Change in Accounting Principle

As discussed in Note 6 to the consolidated financial statements, the Company has changed its method of accounting for leases as of January 1, 2019 due to the adoption of ASC Topic 842, Leases.

Basis for Opinion

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

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

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

/s/ KPMG

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

Dublin, Ireland
March 12, 2021

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

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 14,508	$ 4,801
Prepaid expenses and other current assets	6,904	6,887
Current portion of restricted cash	60	30
Total current assets	21,472	11,718
Property and equipment, net	421	572
Restricted cash, less current portion	248	60
Other assets	10,651	13,401
Total assets	$ 32,792	$ 25,751
Liabilities and Shareholders' Deficit		
Current liabilities:		
Accounts payable	$ 816	$ 15,486
Accrued expenses	1,829	12,458
Derivative liability	28,865	—
Current portion of long-term debt	6,374	5,800
Current portion of royalty-linked notes	114	—
Other current liabilities	3,598	3,042
Income taxes payable	102	200
Total current liabilities	41,698	36,986
Long-term debt, less current portion	22,462	7,625
Royalty-linked notes, less current portion	13,389	—
Other liabilities	5,802	7,378
Total liabilities	$ 83,351	$ 51,989
Commitments and contingencies *(Note 13)*		
Shareholders' deficit:		
Undesignated preferred shares, $0.01 par value per share: 100,000,000 shares authorized at December 31, 2020 and December 31, 2019; no shares issued at December 31, 2020 and December 31, 2019	—	—
Ordinary shares, $0.01 par value per share: 150,000,000 shares authorized, 49,431,028 shares issued at December 31, 2020; 50,000,000 shares authorized, 14,868,973 shares issued at December 31, 2019	494	149
Additional paid-in capital	235,876	208,536
Accumulated deficit	(286,929)	(234,923)
Total shareholders' deficit	(50,559)	(26,238)
Total liabilities and shareholders' deficit	$ 32,792	$ 25,751

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,		
	2020	2019	2018
Revenue	$ —	$ 37	$ 869
Operating expenses:			
Research and development	(21,074)	(90,774)	(68,647)
General and administrative	(11,052)	(11,284)	(8,781)
Total operating expenses	(32,126)	(102,058)	(77,428)
Operating loss	(32,126)	(102,021)	(76,559)
Interest expense, net	(15,097)	(861)	(426)
Financing transaction costs	(2,848)	—	—
Adjustments to fair value of derivatives	(1,745)	—	—
Extinguishment of debt	340	—	—
Other income, net	213	196	401
Total other expense	(19,137)	(665)	(25)
Loss before income taxes	(51,263)	(102,686)	(76,584)
Income tax expense	(743)	(444)	(472)
Net loss and comprehensive loss	(52,006)	(103,130)	(77,056)
Net loss attributable to ordinary shareholders	$ (52,006)	$ (103,130)	$ (77,056)
Net loss per share attributable to ordinary shareholders – basic and diluted	$ (2.17)	$ (7.10)	$ (8.82)
Weighted average ordinary shares outstanding – basic and diluted	24,009,818	14,518,036	8,734,109

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

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

	Convertible Preferred Shares		Ordinary Shares		Additional Paid in Capital	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount			
Balance at December 31, 2017	5,686,663	$ 57	413,110	$ 4	$ 94,227	$ (54,737)	$ 39,494
Issuance of Series B convertible preferred shares, net of issuance costs	1,709,650	17	—	—	32,159	—	32,159
Issuance of ordinary shares on initial public offering, net of issuance costs	—	—	6,350,000	64	74,089	—	74,153
Exercise of share options	—	—	2,008	—	7	—	7
Issuance of ordinary shares under subscription agreement	—	—	190,615	2	1,360	—	1,362
Redenomination of share capital	—	42	—	(42)	—	—	(42)
Conversion of preferred shares to ordinary shares	(7,396,313)	(116)	7,396,313	116	—	—	116
Issuance of warrants for ordinary shares	—	—	—	—	139	—	139
Share-based compensation expense	—	—	—	—	1,290	—	1,290
Net loss	—	—	—	—	—	(77,056)	(77,056)
Balance at December 31, 2018	—	$ —	14,352,046	$ 144	$ 203,271	$ (131,793)	$ 71,622
Issuance of ordinary shares in conjunction with vesting of restricted share units	—	—	36,924	—	—	—	—
Exercise of share options	—	—	18,232	—	60	—	60
Issuance of ordinary shares under subscription agreement	—	—	461,771	5	3,032	—	3,037
Share-based compensation expense	—	—	—	—	2,173	—	2,173
Net loss	—	—	—	—	—	(103,130)	(103,130)
Balance at December 31, 2019	—	$ —	14,868,973	$ 149	$ 208,536	$ (234,923)	$ (26,238)
Issuance of ordinary shares, net	—	—	34,562,055	345	12,987	—	13,332
Share-based compensation expense	—	—	—	—	2,759	—	2,759
Issuance of warrants for ordinary shares	—	—	—	—	11,594	—	11,594
Net loss	—	—	—	—	—	(52,006)	(52,006)
Balance at December 31, 2020	—	$ —	49,431,028	$ 494	$ 235,876	$ (286,929)	$ (50,559)

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,		
	2020	**2019**	**2018**
Cash flows from operating activities:			
Net loss	$ (52,006)	$ (103,130)	$ (77,056)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation	161	152	136
Share-based compensation expense	2,759	2,173	1,290
Gain on short term investments	—	(125)	(423)
Non-cash gain on short term investments	—	—	(278)
Interest on short-term investments	—	(5)	(40)
Amortization of debt discount and deferred financing costs	10,929	362	360
Interest on exchangeable notes - non-cash	3,180	—	—
Financing transaction costs included in financing activities	2,848	—	—
Adjustments to fair value of derivatives	1,745	—	—
Extinguishment of debt	(340)	—	—
Other	752	752	362
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	1,671	2,471	(3,613)
Other assets	308	(1,166)	(2,273)
Accounts payable	(14,671)	11,446	849
Accrued expenses	(10,628)	5,851	3,072
Income taxes	(120)	123	120
Other liabilities	(1,116)	(826)	242
Net cash used in operating activities	(54,528)	(81,922)	(77,252)
Cash flows from investing activities:			
Purchases of property and equipment	(11)	(24)	(90)
Purchases of short-term investments	—	—	(96,493)
Proceeds from sale of short-term investments	—	40,125	87,925
Net cash (used in) / provided by investing activities	(11)	40,101	(8,658)
Cash flows from financing activities:			
Proceeds from PPP Loan	744	—	—
Repayments of long-term debt	(6,233)	(1,034)	—
Proceeds from private placement and rights offering, net of transactions costs	45,038	—	—
Proceeds from issuance of ordinary shares, net of transaction costs	24,926	3,037	1,362
Proceeds from issuance of debt, net of debt issuance costs	—	—	14,507
Proceeds from issuance of Series B convertible preferred shares	—	—	32,175
Proceeds from issuance of ordinary shares on initial public offering, net of issuance costs	—	—	74,153
Proceeds from exercise of share options	—	60	7
Net cash provided by financing activities	64,475	2,063	122,204
Effect of exchange rates on cash and cash equivalents	(11)	(22)	(108)
Net increase / (decrease) in cash, cash equivalents and restricted cash	9,925	(39,780)	36,186
Cash, cash equivalents and restricted cash, at beginning of period	4,891	44,671	8,485
Cash, cash equivalents and restricted cash, at end of period	$ 14,816	$ 4,891	$ 44,671
Supplemental Disclosure of Cash Flow Information:			
Income tax paid—U.S.	$ 120	$ 414	$ 352
Interest paid	996	1,399	809

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

(1) Nature of Operations and Basis of Presentation

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

Since inception, the Company has devoted substantially all of its efforts to research and development, recruiting management and technical staff, and raising capital, and has financed its operations through the issuance of ordinary and convertible preferred shares, debt raised under a financing arrangement with Silicon Valley Bank (SVB) 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 and subsequent 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 RLNsand, 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.

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

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

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

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

principal amount of RLNs to a group of accredited investors (the Private Placement). The Securities were sold in units (the Units) in the Private Placement and Rights Offering with each Unit consisting of an Exchangeable Note in the original principal amount of $1,000 and 50 RLNs. In connection with the Private Placement, the Company agreed to undertake a rights offering of subscription rights to purchase additional Units (the Rights Offering). Under the Rights Offering, the Company and Iterum Bermuda, distributed to the Company's eligible holders of ordinary shares and eligible warrant holders one non-transferable subscription right for each ordinary share owned (or deemed owned in the case of eligible warrant holders) as of the close of business on the record date, August 5, 2020. The subscription period for the Rights Offering expired on August 31, 2020 and right holders subscribed for 220 units. As a result, on September 8, 2020, Iterum Bermuda issued and sold approximately $0.2 million aggregate principal amount of Exchangeable Notes and $0.02 million aggregate principal amount of RLNs. The Units were sold at a price of $1,000 per Unit . 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 1,286.1845 shares per $1,000 principal and interest on the Exchangeable Notes (equivalent to an exchange price of approximately $0.7775 per ordinary share) as of November 2, 2020, which was adjusted from the initial exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $1.00 per ordinary share) and is subject to further adjustment pursuant to the terms and conditions of the indenture governing the Exchangeable Notes. The RLNs entitle holders to payments based on a percentage of the Company's net revenues from potential U.S. sales of specified sulopenem products, subject to the terms and conditions of the indenture governing the RLNs. Pursuant to the indenture governing the RLNs, the payments on the RLNs will be up to either 15% or 20 % of net revenues from U.S. sales of such products, depending on the indication approved by the U.S. Food and Drug Administration (the FDA). The aggregate amount of payments on each RLN is capped at $160.00 (or 4,000 times the principal amount of such RLN). Iterum Bermuda received net proceeds from the sale of the Securities of approximately $45.0 million, after deducting placement agent fees and offering expenses.

In April 2020, the Company began deferring payment on its share of U.S. payroll taxes owed, as allowed by the Coronavirus Aid, Relief and Economic Security Act (CARES Act) through December 31, 2020. The Company is able to defer half of its share of U.S. payroll taxes owed until December 31, 2021, with the remaining half due on December 31, 2022. On April 3, 2020, the U.S. Small Business Administration (SBA) launched a Paycheck Protection Program (the Program) established following the signing of the CARES Act on March 27, 2020. On April 30, 2020, the Company's wholly owned subsidiary, Iterum Therapeutics US Limited, (the Borrower) entered into the PPP loan with SVB (the Lender) under the Program, pursuant to the Company 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 shall be no payments due by the Company until the SBA remits the forgiveness amount to the borrower or 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 will be 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, and the remaining loan of $404 began amortization in December with equal monthly repayments of $26 through March 2022.

On June 3, 2020, the Company entered into a Securities Purchase Agreement (June 3 SPA) with certain institutional investors (the June 3 Purchasers) pursuant to which the Company issued and sold, in a registered direct offering (June 3 Offering), an aggregate of 2,971,770 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $1.6825, for aggregate gross proceeds to the Company 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 the Company. The Company offered the ordinary shares in the June 3 Offering pursuant to its universal shelf registration statement on Form S-3. Pursuant to the June 3 SPA, in a concurrent private placement, the Company issued and sold to the June 3 Purchasers warrants to purchase up to 1,485,885 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $1.62 per ordinary share, subject to adjustment in certain circumstances, and will expire on December 5, 2025. The closing date of the June 3 Offering was June 5, 2020. Warrants to purchase 208,023 ordinary shares, amounting to 7% of the ordinary shares issued under the June 3 SPA, were issued to designees of the placement agent on the closing of the June 3 Offering Upon closing, the warrants issued to such designees were exercisable immediately at an exercise price of $2.1031 per ordinary share, and will expire on June 3, 2025.

On June 30, 2020, the Company entered into a securities purchase agreement (June 30 SPA) with certain institutional investors (the June 30 Purchasers) pursuant to which the Company issued and sold in a registered direct offering (June 30 Offering) an aggregate of 3,372,686 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $1.4825, for aggregate gross proceeds to the Company 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 the Company. The Company offered the ordinary shares in the June 30 Offering pursuant to its universal shelf registration statement on Form S-3. Pursuant to the June 30 SPA, in a concurrent private placement, the Company issued and sold to the June 30 Purchasers warrants to purchase up to 1,686,343 ordinary shares. Upon closing, the warrants were exercisable immediately at an exercise price of $1.42 per ordinary share, subject to adjustment in certain circumstances, and will expire on January 2, 2026. The June 30 Offering closed on July 2, 2020. Warrants to purchase 236,088 ordinary shares, amounting to 7% of the ordinary shares issued under the June 30 SPA, were issued to designees of the placement agent on closing of the June 30

Offering. Upon closing, the warrants issued to such designees were exercisable immediately at an exercise price of $1.8531 per ordinary share, and will expire on June 30, 2025.

On October 27, 2020, the Company completed a registered public offering (the October Offering) in which it sold an aggregate of (i) 15,511,537 ordinary shares, $0.01 nominal value per share, (ii) pre-funded warrants exercisable for an aggregate of 11,411,539 ordinary shares and (iii) warrants exercisable for an aggregate of 20,192,307 ordinary shares. The pre-funded warrants were issued and sold to certain purchasers whose purchase of ordinary shares in the October 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 the Company's outstanding ordinary shares immediately following the consummation of the October 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 $0.65 per ordinary share and warrant and $0.64 per pre-funded warrant and warrant. The Company's net proceeds from the October Offering, after deducting placement agent fees and other estimated offering expenses payable by the Company, were approximately $15.5 million. The warrants are exercisable upon issuance at a price of $0.65 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 $0.01 per ordinary share, subject to adjustment in certain circumstances, and expire when exercised in full, subject to certain conditions. As of December 31, 2020, all pre-funded warrants had been exercised for net proceeds of $0.11 million. In connection with the October Offering, the Company entered into a Securities Purchase Agreement (the Purchase Agreement) on October 22, 2020 with certain institutional investors. The Purchase Agreement contains customary representations and warranties of the Company, termination rights of the parties, and certain indemnification obligations of the Company and ongoing covenants of the Company, including a prohibition on the Company entering into variable rate transactions for a period of 12 months after the closing of the October Offering, subject to certain exceptions. Warrants to purchase 1,884,615 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 Offering, were issued to designees of the placement agent on closing of the October Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $0.8125 per ordinary share and will expire on October 22, 2025.

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, 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 $52,006, $103,130 and $77,056 for the years ended December 31, 2020, 2019 and 2018, respectively. The Company had an accumulated deficit of $286,929 as of December 31, 2020 and expects to continue to incur net losses for the foreseeable future. Management believe that its cash and cash equivalents balance of $14,508 at December 31, 2020, the net proceeds of $42,096 from the underwritten public offering which closed on February 8, 2021, including the exercise of the underwriter's option in full to purchase additional shares, which closed on February 10, 2021, and the net proceeds of $32,200 from the registered direct offering which closed on February 12, 2021 are sufficient to fund operations for at least one year from the date the consolidated financial statements are issued. In making this assessment management have considered the planned operations of the company and the ability to adjust its plans if required.

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, a sale of the Company, a merger or other business combination 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.

COVID-19 Global Pandemic

The global impact of the COVID-19 pandemic has caused a disruption of the normal operations of many businesses, including the temporary closure or scale-back of business operations and/or the imposition of either quarantine or remote work or meeting requirements for employees, either by government order or on a voluntary basis. The pandemic may impact the ability of the

Company's strategic partners to operate and fulfill their contractual obligations, and result in an increase in their costs and cause delays in performance. These effects, and the direct effect of the virus and any potential disruption on the Company's operations, may negatively impact the Company's ability to meet its strategic targets. The Company's employees, in most cases, are working remotely due to safety concerns and using various technologies to perform their functions. Additionally, the disruption and volatility in the global and domestic capital markets may increase the cost of capital and limit the Company's ability to access capital. Both the health and economic aspects of COVID-19 are highly fluid and the future course of each is uncertain. For these reasons and other reasons that may come to light if the coronavirus pandemic and associated protective or preventative measures expand, the Company may experience a material adverse effect on its business operations and financial condition; however, its ultimate impact is highly uncertain and subject to change.

The Company cannot foresee if and when the outbreak of COVID-19 will be effectively contained, nor can the Company predict the severity and duration of its impact. Covid-19 has not yet had a significant impact on the Company's day to day operations. Management is actively monitoring the global situation on its financial condition, liquidity, operations, suppliers, industry, and workforce. Given the daily evolution of the COVID-19 outbreak and the global responses to curb its spread, the Company is not able to estimate the adverse effects of the COVID-19 outbreak on its results of operations, financial condition, or liquidity.

(2) Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual for research and development expenses, the valuation of restricted ordinary shares, the valuation of share-based compensation awards the valuation of the RLNs and the Derivative liabilities. 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. The Company has contemplated the impact of COVID-19 within its financial statements and is not aware of any specific event or circumstance that would require the Company to update estimates, judgments or revise the carrying value of any assets or liabilities.

Specifically, management has estimated variables used to calculate the discounted cash flow analysis (DCF) and assumptions used in the Black-Scholes and binomial lattice models to value derivative instruments (see Note 3 - Fair Value of Financial Assets and Liabilities).

Comprehensive Loss

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

Consolidation

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

Short-term Investments

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

(In thousands, except share and per share data)

Cash and Cash Equivalents

The Company's cash and cash equivalents consist of cash balances and highly liquid investments with maturities of three months or less at the date of purchase. Accounts held at U.S. financial institutions are insured by the FDIC up to $250, while accounts held at Irish financial institutions are insured under the Deposit Guarantee Scheme up to $122 (€100).

Cash accounts with any type of restriction are classified as restricted cash. If restrictions are expected to be lifted in the next twelve months, the restricted cash account is classified as current. Included within restricted cash on the Company's consolidated balance sheet is a certificate of deposit for $90 which is being held by a third party bank as collateral for the irrevocable letter of credit issued in March 2018 to secure an office lease (see Note 6 – Leases). Also included within restricted cash on the Company's consolidated balance sheet is $17 relating to the warrants issued on June 5, 2020 pursuant to the June 3 SPA, $19 relating to the warrants issued on July 2, 2020 pursuant to the June 30 SPA and $182 relating to warrants issued in the October Offering. On the closing date of each of the June 3 Offering, June 30 Offering and October 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.

Property and Equipment

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

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

Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in loss from operations. Repairs and maintenance costs are expensed as incurred. The Company reviews the recoverability of all long-lived assets, including the related useful life, whenever events or changes in circumstances indicate that the carrying amount of a long-lived asset might not be recoverable.

Leases

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

Research and Development Expenses

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

Accrued Research and Development Expenses

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

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

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

Patent Costs

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

Share-Based Compensation

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

The Company measures share-based awards granted to employees and directors with both performance and service based vesting conditions based on the fair value on the date of grant using the Monte Carlo simulation model. Compensation expense of

those awards is recognized over the determined vesting period, the period over which all the specified vesting conditions are to be satisfied, using the straight-line method.

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

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

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

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

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

Grant Awards

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

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

The Company recognized the CARB-X award as revenue, rather than as a reduction of research and development expenses, because the Company was the principal in conducting the research and development activities and this contract was central to its ongoing operations. Revenue was recognized as the qualifying expenses related to the contract were incurred. Five steps are applied in the revenue recognition process: (1) identify the contract with a customer; (2) identify the performance obligation in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligations in the contract; and (5) recognize revenue when (or as) the entity satisfies the performance obligation. Revenue recognized upon incurring qualifying expenses in advance of receipt of funding is recorded in the Company's consolidated balance sheet as other prepaid assets. The related costs incurred by the Company were included in research and development expenses in the Company's consolidated statements of operations and comprehensive loss. No revenue was recognized for the year ended December 31, 2020. The Company recognized $37 and $869 as revenue for the years ended December 31, 2019 and 2018, respectively, in respect of the CARB-X award.

Research and Development Credits

Research and development credits are available to the Company under the tax laws in both Ireland and the 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 advance payments to a supplier, debt, Exchangeable Notes and Derivative liability are carried at fair value, determined according to the fair value hierarchy above, see Note 3 for further details. The carrying amounts reported in the consolidated balance sheets for prepaid expenses and other current assets, accounts payable 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 accounts 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 are revalued each reporting period with the resulting change in fair value reflected in other (expense) / income, net.

In determining the appropriate fair values, the Company uses a variety of valuation techniques applying DCF, Black-Scholes and binomial lattice models, which are discussed in Note 3 – Fair Value of Financial Assets and Liabilities. The Company's 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.

Royalty-Linked Notes

The RLNs qualify as debt instruments under ASC 470, *Debt*, and are initially recorded at fair value, applying a DCF model, and then subsequently measured at amortized cost . The Company assesses the valuation of this debt for any significant changes to the facts and circumstances in the initial valuation which would impact the carrying value, and if required, make adjustments to revalue the debt as appropriate. Amortization is recognized as interest expense over the term of the debt instrument using the effective interest method.

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's June 3 Offering, June 30 Offering and October Offering contain 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 and cash equivalents. The Company has most of its cash and cash equivalents at two accredited financial institutions in the United States and Ireland, in amounts that exceed federally insured limits. The Company did not hold any short-term investments as of December 31, 2020. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Income Taxes

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

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

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

On December 22, 2017, the United States federal government enacted the Tax Act, marking a change from a worldwide tax system to a modified territorial tax system in the United States. As part of this change, the Tax Act, among other changes, provided a reduction of the U.S. federal corporate income tax rate from 34% to 21%, an indefinite carryforward of net operating losses incurred in 2018 and future periods, and an interest limitation starting in 2018 with an indefinite carryforward. Any impact to the Company related to these items was accounted for in the 2018, 2019 and 2020 tax provisions with minimal impact.

The CARES Act lifts certain deduction limitations originally imposed by the Tax Cuts and Jobs Act of 2017 (2017 Tax Act). Corporate taxpayers may carryback net operating losses (NOLs) originating during 2018 through 2020 for up to five years, which was not previously allowed under the 2017 Tax Act. The CARES Act also eliminates the 80% of taxable income limitations by allowing corporate entities to fully utilize NOL carryforwards to offset taxable income in 2018, 2019 or 2020. Taxpayers may generally deduct interest up to the sum of 50% of adjusted taxable income plus business interest income (30% limit under the 2017 Tax Act) for tax years beginning January 1, 2019 and 2020. The CARES Act allows taxpayers with alternative minimum tax credits to claim a refund in 2020 for the entire amount of the credits instead of recovering the credits through refunds over a period of years, as originally enacted by the 2017 Tax Act. The enactment of the CARES Act did not result in any material adjustments to the Company’s income tax provision for the year ended December 31, 2020, or to the Company’s net deferred tax assets as of December 31, 2020.

Net Loss Per Ordinary Share

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

(In thousands, except share and per share data)

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

	Year ended December 31,		
	2020	2019	2018
Options to purchase ordinary shares	953,377	1,150,270	665,219
Unvested restricted ordinary shares	—	—	86,068
Unvested restricted share units	—	31,367	36,924
Unvested performance restricted share units	983,000	50,000	—
Warrants	24,444,292	19,890	19,890
Total	26,380,669	1,251,527	808,101

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

Segment and Other Information

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

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

	Year ended December 31,		
Operating expenses	2020	2019	2018
Ireland	$ 23,423	$ 90,792	$ 66,552
U.S.	8,703	11,266	10,876
Total	$ 32,126	$ 102,058	$ 77,428

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

Long lived assets	December 31, 2020	December 31, 2019
Ireland	$ 8,101	$ 10,936
U.S.	2,971	3,037
Total	$ 11,072	$ 13,973

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 not required to make a top-heavy contribution for the years ended December 31, 2020 and 2019. The Company made a contribution of $114 for the year ended December 31, 2018.

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 hadno inventory as of December 31, 2020 or December 31, 2019.

Contingent Consideration

Certain license agreements contain milestone payments that could result in the requirement to make contingent consideration payments, see Note 13 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, 2020, no milestones had been met that required the Company to recognize contingent consideration.

Recently Adopted Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13,*Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments.* The new guidance within ASU 2016-13, along with related updates (collectively ASC 326) introduces an approach based on expected losses to estimate credit losses on certain types of financial instruments by using all practical and relevant information. The new guidance became effective for annual periods beginning after December 15, 2019, and interim periods within those annual periods. Further clarification on disclosures relating to the standard were released in March 2020, in ASU 2020-03, *Codification Improvements to Financial Instruments*, which outlined seven areas of improvements relating to financial instrument guidance. The new standards were effective January 1, 2020 and adoption did not have a material impact on the Company's consolidated financial statements

In August 2018, the FASB issued ASU No. 2018-13,*Fair Value Measurement (Topic 820): Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement.* This standard modifies certain disclosure requirements on fair value measurements. This standard became effective for the Company on January 1, 2020, and did not have a material impact on the Company's disclosures.

Recent Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12,*Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* The new guidance is intended to simplify the accounting for income taxes by removing certain exceptions and by updating accounting requirements around franchise taxes, goodwill recognized for tax purposes, the allocation of current and deferred tax expense among legal entities, among other minor changes. ASU 2019-12 is effective for fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. Early adoption is permitted. The Company is assessing what impact ASU 2019-12 will have on the consolidated financial statements.

In January 2020, the FASB issued ASU 2020-01,*Investments-Equity Securities (Topic 321), Investments-Equity Method and Joint Ventures (Topic 323), and Derivatives and Hedging (Topic 815): Clarifying the Interactions between Topic 321, Topic 323, and Topic 815.* The amendments in ASU 2020-01 clarify the interaction of the accounting for equity securities under Topic 321 and investments accounted for under the equity method of accounting. ASU 2020-01 is effective for fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. Early adoption is permitted. The Company is assessing what impact ASU 2020-01 will have on the consolidated financial statements.

In August 2020, the FASB issued ASU 2020-06,*Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity,* which reduces the number of accounting models for convertible instruments and allows more contracts to qualify for equity classification. The ASU is effective for annual and interim periods in fiscal years beginning after December 15, 2021. Early adoption is permitted, but no earlier than annual and interim periods in fiscal years beginning after December 15, 2020. The Company is assessing what impact ASU 2020-06 will have on the consolidated financial statements.

In October 2020, the FASB issued ASU 2020-10,*Codification Improvements,* which clarifies various topics in the Codification by providing consistency in codification wording and moving existing disclosure requirements to the relevant disclosure sections. ASU 2020-10 is effective for annual and interim periods in fiscal years beginning after December 15, 2020. Early adoption is permitted. The Company is assessing what impact ASU 2020-10 will have on the consolidated financial statements.

(In thousands, except share and per share data)

(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, 2020 and December 31, 2019 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value.

December 31, 2020 Assets	Total	Level 1	Level 2	Level 3
Other assets – advance payment to supplier	3,357	—	—	3,357

December 31, 2019 Assets	Total	Level 1	Level 2	Level 3
Other assets – advance payment to supplier	3,884	—	—	3,884

The other asset above relates to advance payments made to a supplier that were recorded at fair value using DCF analysis as of December 31, 2020 and December 31, 2019. The fair value measurements of these advance payments were determined based on significant unobservable inputs, including a discount rate of 21% and 15%, as of December 31, 2020 and December 31, 2019, respectively, and the expected time to recovery of the payment. Changes to the inputs described above are not expected to have a material impact on the Company's financial position and results of operations in any given period.

The carrying amounts reported in the consolidated balance sheets for prepaid expenses and other current assets, accounts payable, accrued expenses and other current liabilities approximate their fair value based on the short-term maturity of these instruments.

The following table presents information about the Company's debt, Exchangeable Notes, Derivative liability and RLNs. The Company's long-term debt was carried at amortized cost on the consolidated balance sheet as of December 31, 2020 and December 31, 2019 and indicates the fair value hierarchy of the valuation inputs utilized to determine the approximate fair value.

December 31, 2020 Liabilities	Book Value	Approximate Fair Value	Level 1	Level 2	Level 3
Debt					
Current portion of long-term debt	$ 6,374	$ 6,374	—	6,374	—
Long-term debt, less current portion	1,626	1,512	—	1,512	—
Exchangeable Notes					
Long-term exchangeable note	20,836	31,493	—	31,493	—
Derivative liability - exchange option and change of control	28,865	28,865	—	—	28,865
Revenue Futures					
Current portion of royalty-linked notes	114	114	—	—	114
Long-term royalty-linked notes, less current portion	13,389	16,379	—	—	16,379
Total	$ 71,204	$ 84,737	—	$ 39,379	$ 45,358

December 31, 2019 Liabilities	Book Value	Approximate Fair Value	Level 1	Level 2	Level 3
Current portion of long-term debt	$ 5,800	$ 5,800	—	5,800	—
Long-term debt, less current portion	7,625	7,213	—	7,213	—
Total	$ 13,425	$ 13,013	—	13,013	—

The book value of the current portion of long-term debt approximates its fair value due to the short-term nature of the balance. The fair value of long-term debt, less current portion was determined based on a DCF analysis using quoted market interest rates, without consideration of transaction costs, which represents a Level 2 basis of fair value measurement. The counterparty to the long-term debt is a major international financial institution.

The Level 3 liabilities held as of December 31, 2020 consist of the embedded exchange option and change of control premium contained in the Exchangeable Notes (see Note 8 - Debt) and a separate financial instrument, that was issued as part of the Units, the RLNs (see Note 9 – 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 are 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 Derivative liability, representing the exchange option and change of control premium, was recorded at a fair

(In thousands, except share and per share data)

value of $27,038 at January 21, 2020 and the fair value of the Derivative liability related to the Rights Offering was $82. The fair value of the exchange option and change of control premium at December 31, 2020 amounted to $21,237 and $7,628, respectively. 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 1,286.1845 shares per $1,000 principal and interest on the Exchangeable Note (equivalent to an exchange price of approximately $0.7775 per ordinary share) as of November 2, 2020, what was adjusted from the initial exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $1.00 per ordinary share and is subject to further adjustment pursuant to the terms of the indenture governing the Exchangeable Notes.

In the event of a fundamental change that is not a liquidation event (Fundamental Change), under the indenture governing the Exchangeable Note, the Company will be required to pay the holders of the Exchangeable Notes the greater of three times the outstanding principal amount of such Exchangeable Notes and the consideration that would be received by the holders of such Exchangeable Notes, in connection with such Fundamental Change, if the holders had exchanged their notes 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 $7,628 at December 31, 2020.

The fair value of each component of the Derivative liability was determined using a valuation technique applying DCF analysis or Black-Scholes in combination with binomial lattice models, 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, 2020 include the indenture terms of the Exchangeable Notes, the Company's share price at the exchange date, the expected annual volatility of the Company's ordinary shares, management's assumption regarding the probability of a fundamental change pursuant to the terms of the indenture governing the Exchangeable Notes, and a risk-adjusted discount 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 for the year ended December 31, 2020:

Balance at December 31, 2019	$ —
Initial fair value upon issuance of the Exchangeable Notes in the Private Placement	27,038
Fair value added upon issuance of Exchangeable Notes in the Rights Offering	82
Adjustment to fair value	1,745
Balance at December 31, 2020	$28,865

The following summary table shows the assumptions used in the Black-Scholes and binomial lattice pricing models to estimate the fair value of the exchange option:

	December 31, 2020	January 21, 2020 (Issuance Date)
Expected term in years	4.04	4.98
Volatility	120%	80%
Risk-free interest rate	0.26%	1.57%
Dividend rate	0%	0%
Discount rate	21%	21%

The significant assumptions used in the DCF model, to estimate the fair value of the change of control feature at December 31, 2020, were a discount rate of 21% and management's assumption regarding the probability of a fundamental change pursuant to the terms of the indenture governing the Exchangeable Notes.

The RLN liability is carried at amortized cost on the consolidated balance sheet as of December 31, 2020 (see Note 9 – Royalty-Linked Notes). The book value of the current portion of the RLN liability approximates its fair value due to the short-term nature of the balance. The total fair value of $16,493 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 indenture terms of the RLNs, 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 21%. 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.

(In thousands, except share and per share data)

(4) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following:

	December 31, 2020	December 31, 2019
Refundable FDA filing fee (1)	$ 2,876	-
Short-term deposits	2,360	1,139
Research and development tax credit receivable	801	1,036
Prepaid research and development expenses	157	1,679
Prepaid insurance	415	569
Value added tax receivable	64	68
Other prepaid assets	231	57
Deferred financing expenses	—	2,339
Total	$ 6,904	$ 6,887

(1) FDA filing fee refund of $2,876 was received in January 2021

(5) Property and Equipment, net

Property and equipment and related accumulated depreciation are as follows:

	December 31, 2020	December 31, 2019
Leasehold improvements	$ 592	$ 592
Furniture and fixtures	120	120
Laboratory equipment	86	81
Computer equipment	137	132
	935	925
Less: accumulated depreciation	(514)	(353)
	$ 421	$ 572

Depreciation expense was $161, $152 and $136 for the years ended December 31, 2020, 2019 and 2018, respectively.

(6) Leases

In February 2016, the FASB issued ASU 2016-02,*Leases* (Topic 842) in order to increase transparency and comparability among organizations by recognizing lease assets and lease liabilities on the balance sheet for those leases classified as operating leases under prior GAAP. In July 2018, the FASB issued ASU 2018-11 *Leases* (Topic 842): *Targeted Improvements* which provides the option to adopt the standard retrospectively for each prior period presented, as initially set out in ASU 2016-02, or as of the adoption date with a cumulative-effect adjustment to the opening balance of retained earnings. In March 2019, the FASB issued ASU 2019-03 *Leases* (Topic 842): *Codification Improvements* amending the transition disclosures for Topic 842, in that all companies are exempt from certain interim period transition disclosure requirements. ASU 2016-02 requires a lessee to recognize a liability to make lease payments (the lease liability) and a right-of-use asset, representing its right to use the underlying asset for the lease term, on the balance sheet. The Company adopted ASU 2016-02 in the first quarter of 2019 utilizing the modified retrospective transition method with an effective date as the date of initial application. Consequently, prior period balances and disclosures have not been restated. The adoption of ASU 2016-02 on January 1, 2019 resulted in the recognition of right-of-use assets of $7.6 million and operating lease liabilities of $7.8 million, however, the adoption of the standard did not have an impact on the Company's beginning retained earnings, results from operations or cash flows.

The Company has entered into a number of operating leases, primarily for office space and commercial property. These leases have terms which range from one to 18 years, and generally include one or more options to terminate or renew. The termination option can reduce the lease term for a period of 10 years, however the remaining lease term does not represent this early termination date as management has concluded that it is reasonably certain that the Company will not exercise this option. The renewal terms can extend the lease term for additional periods ranging from three to five years. These renewal options are represented in the remaining lease term as management has concluded that it is reasonably certain that the Company will exercise the renewal option. Certain leases contain variable lease payments, including payments based on an index or rate. Variable lease payments based on an index or rate are initially measured using the index or rate in effect at lease commencement. Certain agreements contain both lease and non-lease components. The Company has elected to separately account for these components in determining the lease liabilities and right-of-use

(In thousands, except share and per share data)

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. Termination notice has been given on one lease which will now expire inone year rather than six. The right-of-use asset and lease liability have accordingly been reduced for this amendment.In September 2020, the Company entered into a sub-lease agreement for a commercial unit that extends through September 2023. The Company recognized $991 and $1,015 of operating lease costs for right-of-use assets during the years ended December 31, 2020 and 2019, respectively. The Company recognized $118 of sublease income during the year ended December 31, 2020. The Company was not party to any sublease agreement during the year ended December 31, 2019.

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

	December 31, 2020	December 31, 2019
Cash paid for operating lease liabilities	$ 1,116	$ 826
Right-of-use assets obtained in exchange for new operating lease obligation (1)	—	7,622

(1) All operating lease included above were held at January 01, 2019

	December 31, 2020	December 31, 2019
Weighted-average remaining lease term	13.2 years	12.5 years
Weighted-average discount rate	7.5 %	7.6 %

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

	December 31, 2020	December 31, 2019
Other assets	$5,261	$7,144
Other current liabilities	$573	$580
Other liabilities	5,172	6,748
Total lease liabilities	$5,745	$7,328

The Company has recorded the reduction in carrying amount of the right-of-use assets and the change in the lease liability in the Other category within the operating section of the consolidated statement of cash flows.

Future lease payments included in the measurement of lease liabilities on the consolidated balance sheet as of December 31, 2020 for the following five fiscal years and thereafter were as follows:

Due in 12 month period ended December 31,	
2021	$962
2022	736
2023	741
2024	745
2025	675
Thereafter	4,791
	$8,650
Less imputed interest	(2,905)
Total lease liabilities	$5,745

(In thousands, except share and per share data)

(7) Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2020	December 31, 2019
Accrued payroll and bonus expenses	$ 966	$ 1,207
Accrued other expenses	614	1,249
Accrued clinical trial costs	144	9,866
Accrued manufacturing expenses	105	136
Total	$ 1,829	$ 12,458

(8) 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. A non-utilization fee of 1.50% of the aggregate undrawn principal amount was to apply if the Company satisfied the above conditions but chose not to draw down the second term loan. The Company did not satisfy the conditions for the second draw above before the deadline of October 31, 2019.

Required monthly amortization payments for the initial $15,000 draw commenced on November 1, 2019 and total principal repayments of $6,207 were made during the year ended December 31, 2020. Interest accrues at a floating per annum rate equal to the greater of (i) 8.31%; or (ii) 3.89% above the Wall Street Journal prime rate, and is payable monthly in arrears. All outstanding principal, plus a 4.20% final interest payment, will be due and payable on the earliest to occur of March 1, 2022 (the maturity date), the acceleration of the term loan or the prepayment of the term loan. The final payment fee of $630 which represents 4.2% of the funded loan, is accreted using the effective interest method over the life of the loan as interest expense. Voluntary prepayments are permitted at any time, subject to a prepayment fee of 4.00% in the first year, 3.00% in the second year, and 2.00% thereafter.

In connection with the initial $15,000 draw, the Company issued SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B convertible preferred shares (which converted into warrants to purchase 19,890 ordinary shares upon the Company's initial public offering (IPO)) at an exercise price of $18.85 per share. If the second term loan had been drawn down, each of SVB and LSF would have been automatically entitled to purchase additional ordinary shares in an aggregate amount equal to 2.50% of the second term loan divided by the applicable exercise price.

The loan proceeds were allocated based on the relative fair values of the debt instrument and the warrant instrument. The fair value of the warrants and the closing costs were recorded as debt discounts and are being amortized using the effective interest rate method over the term of the loan. The effective annual interest rate of the outstanding debt is approximately 12.51% as of December 31, 2020. The Company recognized $1,355 and $1,761 of interest expense related to the loan agreement during the years ended December 31, 2020 and 2019, respectively, including $404 and $362 related to the accretion of the debt discounts and deferred financing costs during the years ended December 31, 2020 and 2019, respectively.

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 approximately $51.6 million aggregate principal amount of 6.500% Exchangeable Notes and $0.1 million 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 approximately $0.2 million aggregate principal amount of 6.500% Exchangeable Notes and $0.02 million aggregate principal amount of RLNs, to existing shareholders. The Securities were sold in

(In thousands, except share and per share data)

Units with each Unit consisting of an Exchangeable Note in the original principal amount $1,000 and 50 RLNs. The Units were sold at a price of $1,000 per Unit.

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 initial exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $1.00 per ordinary share), which exchange rate was adjusted to 1,286.1845 shares per $1,000 principal and interest on the Exchangeable Note (equivalent to an exchange price of approximately $0.7775 per ordinary share) as of November 2, 2020 and is subject to further adjustment pursuant to the terms of the indenture governing the Exchangeable Notes. 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.

In addition, the Exchangeable Notes will become due and payable by the Company upon the occurrence of a Fundamental Change as defined in the indenture governing the Exchangeable Notes. The Company will be required to pay the holders of the Exchangeable Notes the greater of three times the outstanding principal amount of such Exchangeable Notes and the consideration that would be received by the holders of such Exchangeable Notes in connection with such Fundamental Change if the holders had exchanged their notes 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 $3,180 of interest expense related to the Exchangeable Notes during the year ended December 31, 2020 and $7,764 related to the amortization of the debt discounts and deferred financing costs during the year ended December 31, 2020. These amounts are recorded in interest expense, net in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2020. The balance of the Exchangeable Notes as of December 31, 2020 is as follows:

	December 31, 2020	
	Principal	Accrued Interest
January 2020 $1,000 Exchangeable Notes exchangeable into ordinary shares at $0.7775 per share, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	$51,588	$3,176
September 2020 $1,000 Exchangeable Notes exchangeable into ordinary shares at $0.7775 per share, 6.5% interest, due January 31, 2025 (2025 Exchangeable Notes)	$220	$4
2025 Exchangeable Notes	51,808	3,180
Unamortized discount and debt issuance costs	(34,152)	—
2025 Exchangeable Notes, net	$17,656	$3,180

Payment Protection Program

On April 3, 2020, the SBA launched the Program following the signing of the CARES Act on March 27, 2020. On April 30, 2020, the Borrower entered the PPP loan with SVB under the 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 shall be no payments due by the Company until after the Deferral Period. Following the Deferral Period, equal monthly repayments of principal and interest will be 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, and the remaining loan of $404 began amortization in December with equal monthly repayments of $26 through March 2022. The Company recognized $1 of interest expense related to the loan agreement during the year ended December 31, 2020.

Scheduled principal payments on outstanding debt, as of December 31, 2020, are as follows:

Year Ending December 31,	
2021	6,516
2022	1,621
2023	—
2024	—
2025	51,808
Thereafter	104
	$60,049

(9) 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 indenture governing the RLNs (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.

In accordance with exceptions allowed under ASC 815-10, *Derivatives and Hedging*, due to a limit on the amount of royalties that the noteholders can earn under the RLN, this transaction is accounted for as a debt liability under ASC 470, *Debt*, that is being amortized using the effective interest method over the life of the arrangement. The Company has no obligation to pay any amount to the noteholders until the net revenue of the specified products are earned. In order to record the amortization of the liability, the Company is required to estimate the total amount of future net revenue to be earned in each period under the RLN Indenture and the payments that will be passed through to the noteholders over the life of the RLN Indenture.

(In thousands, except share and per share data)

The note proceeds from both the Private Placement and subsequent Rights Offering were allocated based on the relative fair value of the debt instrument, less transactions costs amounting to $1,239, as debt discounts. The Company imputes interest on the amortized cost of the liability using an estimated effective interest rate of 31.1% as of December 31, 2020. Payments to the noteholders in each period, related to future sales of sulopenem, would offset the liability. The Company periodically assesses the revenue forecasts of the specified sulopenem products and the related payments, and to the extent such payments are greater or less than the initial estimate, the Company adjusts the amortization of the liability and interest rate, to ensure the liability is fully amortized on fulfilment of the agreement.

The Company recognized $2,761 of interest expense related to RLNs, in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2020 related to the accretion of debt discounts and deferred financing costs. These amounts are recorded in interest expense, net in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2020. The balance of the RLNs as of December 31, 2020 is as follows:

	December 31, 2020
Total liability related to the sale of future royalties, on inception	$10,742
Amortization of discount and debt issuance costs	2,761
Total liability related to the sale of future royalties at December 31, 2020	$13,503
Current Portion	114
Long-term Portion	$13,389

(10) Shareholders' (Deficit) / Equity

The Company's capital structure consists of ordinary shares, undesignated preferred shares and, prior to the completion of the Company's IPO on May 30, 2018, convertible preferred shares with certain rights and privileges summarized below. Under Irish law, the Company is prohibited from allotting shares without consideration. Accordingly, at least the nominal value of the shares issued underlying any 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

The Company was initially incorporated without a cap on its authorized share capital as permitted by the Irish Companies Act. On October 14, 2015, the Company authorized and issued 413,110 ordinary shares with a par value of $0.01 per share (after taking account of the reverse share split and redenomination of the par value of the ordinary shares from $0.01571 (the nominal value resulting from the reverse share split) to $0.01 on May 15, 2018). On March 13, 2018, the Company redenominated its 44,557,606 authorized and 413,110 issued ordinary shares from $0.0001 to $0.001 per share in accordance with section 83(1)(c) of the Irish Companies Act.

On November 18, 2015, the Company increased the authorized ordinary share capital to 3,659,453 shares with a par value of $0.01 per share.

On May 18, 2017, the Company increased the authorized ordinary share capital to 7,956,715 shares with a par value of $0.01 per share.

On February 16, 2018, the Company increased its authorized ordinary shares by 36,600,891 to 44,557,606 ordinary shares with a par value of $0.01 per share.

On May 30, 2018, the Company increased its authorized ordinary shares by 5,442,394 to 50,000,000 ordinary shares of $0.01 each.

On December 14, 2018, Iterum Therapeutics plc (ITP) and Iterum Therapeutics International Limited (ITIL) entered into a subscription agreement with a supplier of ITIL pursuant to which the supplier agreed to subscribe for ordinary shares in ITP in satisfaction of amounts due and owing under certain commercial agreements entered into between the supplier and ITIL (the Subscription Agreement). Pursuant to the terms of the Subscription Agreement, upon receipt by ITIL of a valid invoice from the supplier, ITP can elect to require the supplier to subscribe for ordinary shares in the capital of ITP (up to a maximum of 700,000 ordinary shares in total) to the value of the invoiced amount (a Subscription). On a Subscription, the supplier will direct ITIL to pay ITP such invoiced amount as subscription monies on the supplier's behalf in satisfaction of the invoiced amount.

On December 14, 2018, ITP elected that the supplier subscribe for 190,615 ordinary shares for an aggregate subscription price of $1.36 million (the December Subscription Monies) upon receipt by ITIL of valid invoices up to that amount from the supplier (the Invoiced Amount). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $1.36 million (€1.20 million) to ITP in satisfaction of the supplier's obligation to pay the December Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

On July 15, 2019, ITP elected that the supplier subscribe for 17,222 ordinary shares for an aggregate subscription price of $0.11 million (the July Subscription Monies) upon receipt by ITIL of valid invoices up to that amount from the supplier (the Invoiced Amount). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $0.11 million (€0.10 million) to ITP in satisfaction of the supplier's obligation to pay the July Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

On August 19, 2019, ITP elected that the supplier subscribe for 245,493 ordinary shares for an aggregate subscription price of $1.67 million (the August Subscription Monies) upon receipt by ITIL of valid invoices up to that amount from the supplier (the Invoiced Amount). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $1.67 million (€1.50 million) to ITP in satisfaction of the supplier's obligation to pay the August Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

On September 30, 2019, ITP elected that the supplier subscribe for 199,056 ordinary shares for an aggregate subscription price of $1.26 million (the September Subscription Monies) upon receipt by ITIL of valid invoices up to that amount from the supplier (the Invoiced Amount). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $1.26 million (€1.15 million) to ITP in satisfaction of the supplier's obligation to pay the September Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

On June 3, 2020, the Company entered into the June 3 SPA with the June 3 Purchasers pursuant to which the Company issued and sold, in the June 3 Offering, an aggregate of 2,971,770 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $1.6825, for aggregate gross proceeds to the Company 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 the Company. The closing date of the June 3 Offering was June 5, 2020.

On June 30, 2020, the Company entered into the June 30 SPA with the June 30 Purchasers pursuant to which the Company issued and sold, in the June 30 Offering, an aggregate of 3,372,686 ordinary shares, $0.01 nominal value per share, at a purchase price per share of $1.4825, for aggregate gross proceeds to the Company 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 the Company. The closing date of the June 30 Offering was July 2, 2020. The Company offered the ordinary shares in the June 3 Offering and June 30 Offering pursuant to its universal shelf registration statement on Form S-3.

On October 27, 2020, the Company completed the October Offering in which it sold an aggregate of (i) 15,511,537 ordinary shares, $0.01 nominal value per share, (ii) pre-funded warrants exercisable for an aggregate of 11,411,539 ordinary shares and (iii) warrants exercisable for an aggregate of 20,192,307 ordinary shares. 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 $0.65 per ordinary share and warrant and $0.64 per pre-funded warrant and warrant. Aggregate gross proceeds to the Company from the October Offering were approximately $17.4 million and net proceeds were approximately $15.5 million after deducting fees payable to the placement agent and other estimated offering expenses payable by the Company.

At the Company's annual general meeting of shareholders on June 10, 2020, the Company's shareholders approved an increase of 100,000,000 ordinary shares to the number of authorized ordinary shares and the Company's Articles of Association were amended accordingly. The Company has authorized ordinary shares of 150,000,000 ordinary shares of $0.01 par value each as of December 31, 2020. The holders of ordinary shares are entitled to one vote for each share held. The holders of ordinary shares have no preemptive or other subscription rights, and there are no redemption or sinking fund provisions with respect to such shares

Warrants to purchase Ordinary Shares

In connection with the initial drawdown of the SVB Secured Credit Facility, 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 19,890 ordinary shares upon the Company's IPO) at an exercise price of $18.85 per share.

In connection with the June 3 Offering completed on June 5, 2020, pursuant to the June 3 SPA, in a concurrent private placement, the Company issued and sold to the June 3 Purchasers warrants to purchase up to 1,485,885 ordinary shares. Upon closing,

(In thousands, except share and per share data)

the warrants became exercisable immediately at an exercise price of $1.62 per ordinary share, subject to adjustment in certain circumstances, and will expire onDecember 5, 2025. Warrants to purchase 208,023 ordinary shares, amounting to 7% of the ordinary shares issued under the June 3 SPA, were issued to designees of the placement agent on the closing of the June 3 Offering. Upon closing, the warrants issued to such designees were exercisable immediately at an exercise price of $2.1031 per ordinary share and will expire on June 3, 2025.

The Company has classified the warrants as equity in accordance with ASC 815. The fair value of the warrants were valued at issuance using the Black-Scholes option pricing model with the following assumptions:

	June 5, 2020
Volatility	120%
Expected term in years	2.50 - 2.75
Dividend rate	0%
Risk-free interest rate	0.47%
Share price	$1.53
Fair value of warrants issued	$0.92 -$1.03

In connection with the June 30 Offering completed on July 2, 2020, pursuant to the June 30 SPA, in a concurrent private placement, the Company has also issued and sold to the June 30 Purchasers warrants to purchase up to 1,686,343 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $1.42 per ordinary share, subject to adjustment in certain circumstances, and will expire on January 2, 2026. Warrants to purchase 236,088 ordinary shares, amounting to 7% of the ordinary shares issued under the June 30 SPA, were issued to designees of the placement agent on closing of the June 30 Offering. Upon closing, the warrants issued to such designees were exercisable immediately at an exercise price of $1.8531 per ordinary share and will expire on June 30, 2025.

The Company has classified the warrants as equity in accordance with ASC 815. The fair value of the warrants were valued at issuance using the Black-Scholes option pricing model with the following assumptions:

	July 02, 2020
Volatility	120%
Expected term in years	2.50 - 2.75
Dividend rate	0%
Risk-free interest rate	0.29%
Share price	$1.19
Fair value of warrants issued	$0.69 -$0.78

In connection with the October Offering, the Company issued and sold warrants to purchase up to 20,192,307 ordinary shares. Upon closing, the warrants became exercisable immediately at an exercise price of $0.65 per ordinary share, subject to adjustment in certain circumstances, and will expire on October 27, 2025. Warrants to purchase 1,884,615 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 Offering, were issued to designees of the placement agent on closing of the October Offering. Upon closing, the warrants issued to such designees became exercisable immediately at an exercise price of $0.8125 per ordinary share and expire on October 22, 2025. As of December 31, 2020, 1,268,859 warrants had been exercised for net proceeds of $0.9 million.

The Company has classified the warrants as equity in accordance with ASC 815. The fair value of the warrants were valued at issuance using the Black-Scholes option pricing model with the following assumptions:

	October 27, 2020
Volatility	120%
Expected term in years	5.00
Dividend rate	0%
Risk-free interest rate	0.34%
Share price	$0.49
Fair value of warrants issued	$0.36 -$0.38

Undesignated Preferred Shares

The Company has authorized 100,000,000 undesignated preferred shares of $0.01 par value each as of December 31, 2020. The Directors are authorized by the Company's Articles of Association to determine the rights attaching to the undesignated preferred

shares including rights of redemption, rights as to dividends, rights on winding up and conversion rights. There wereno undesignated preferred shares in issue as of December 31, 2020 or December 31, 2019.

Convertible Preferred Shares

On November 18, 2015, the Company authorized 3,022,915 Series A convertible preferred shares with a par value of $0.01 per share. On the same day, the Company issued 1,514,320 Series A convertible preferred shares for a purchase price of $15.71 per share for: (1) gross cash proceeds of $20,701; (2) the issue of 190,961 convertible preferred shares to Pfizer as part consideration for the license agreement; and (3) the conversion of $90 debt owed by the Company to its founders for a total of 5,728 preferred shares (after taking account of the reverse share split and redenomination of the par value of the convertible preferred shares from $0.01571 (the nominal value resulting from the reverse share split) per share to $0.01 on May 15, 2018). On March 13, 2018, the Company redenominated its 3,032,463 authorized and 3,032,457 issued Series A convertible preferred shares from $0.0001 to $0.001 par value per share in accordance with section 83(1)(c) of the Irish Companies Act.

On December 9, 2016, the Company authorized 9,548 Series A convertible preferred shares with a par value of $0.01 per share.

On December 16, 2016, the Company issued 1,518,137 Series A convertible preferred shares for a purchase price of $15.71 per share for: (1) gross cash proceeds of $20,851; and (2) the issue of an additional 190,961 convertible preferred shares to Pfizer as part consideration for the license agreement.

On May 18, 2017, the Company authorized 2,654,215 Series B-1 convertible preferred shares with a par value of $0.01 per share and 1,042,728 Series B-2 convertible preferred shares with a par value of $0.01 per share (the Series B convertible preferred shares). On the same day, the Company issued 2,654,206 Series B-1 convertible preferred shares for a purchase price of $17.28 per share, for gross cash proceeds of $45,867 (after taking account of the reverse share split and redenomination of the par value of the convertible preferred shares from $0.01571 (the nominal value resulting from the reverse share split) per share to $0.01 on May 15, 2018). On March 13, 2018, the Company redenominated its 4,801,493 authorized and 4,363,856 issued Series B convertible preferred shares from $0.0001 to $0.001 par value per share in accordance with section 83(1)(c) of the Irish Companies Act.

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

On May 30, 2018, immediately prior to the completion of the Company's IPO, holders of convertible preferred shares of Iterum Therapeutics Plc exchanged their preferred shares for ordinary shares of Iterum Therapeutics Plc on a one-for-one basis and all convertible preferred shares were subsequently cancelled.

Prior to the exchange and cancellation of preferred convertible shares on May 30, 2018, the ordinary shares were subordinate to the convertible preferred shares with respect to dividend rights and rights upon liquidation, winding up and dissolution of the Company and the holders of ordinary shares were entitled to liquidation proceeds after all liquidation preferences for the convertible preferred shares were satisfied.

(11) Share-Based Compensation

On November 18, 2015, the Company's Board of Directors adopted and approved the 2015 Equity Incentive Plan (the 2015 Plan), which authorized the Company to grant up to 223,424 ordinary shares in the form of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units and other share awards. The types of share-based awards, including the rights amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors. The purpose of the 2015 Plan is to provide the Company with the flexibility to issue share-based awards as part of an overall compensation package to attract and retain qualified personnel. On May 18, 2017, the Company amended the 2015 Plan to increase the number of ordinary shares available for issuance under the 2015 Plan by 219,605 shares to 443,029 shares.

On March 14, 2018, the Company's Board of Directors adopted and approved the 2018 Equity Incentive Plan (the 2018 Plan), which became effective upon the execution and delivery of the underwriting agreement related to the Company's IPO. No further grants will be made under the 2015 Plan. The ordinary shares underlying any options that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2015 Plan will not be added back to the ordinary shares available for issuance.

The 2018 Plan authorizes the Company to grant up to 1,018,459 ordinary shares in the form of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units, performance share awards, performance cash awards and other share awards. The types of share-based awards, including the amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors. The ordinary shares underlying any options that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2018 Plan will be added back to the ordinary shares available for issuance under the 2018 Plan.

On December 5, 2018, pursuant to powers delegated to it by the Board of Directors of the Company, the Compensation Committee approved an increase in the number of ordinary shares available to be granted pursuant to the 2018 Plan by 4% of the total number of shares of the Company's issued share capital on December 31, 2018, being 574,081 ordinary shares.

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 594,758 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 shares 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 includes an increase of 2,250,000 ordinary shares in the number of ordinary shares reserved for issuance under the 2018 Plan.

Restricted Ordinary Shares

In connection with the Company's formation, 413,110 restricted ordinary shares were issued on October 14, 2015 to the Company's founders at par value. These ordinary shares are subject to various restrictions pursuant to ordinary share purchase agreements between the Company and each founder, including restrictions on transfer and a Company right of repurchase. The restricted ordinary shares were 25% vested as of October 14, 2016 and 1/36th of the remaining restricted ordinary shares vested on a monthly basis thereafter (subject to acceleration of vesting in connection with certain change of control transactions). A change in status occurred on November 18, 2015 when the founders became employees of the Company. The grant date of these shares is now considered to be November 18, 2015 when the fair value was $3.14 per share.

Restricted ordinary shares were fully vested as of December 31, 2019 and there was no restricted ordinary share activity for the year ended December 31, 2020.

The Company recorded share-based compensation expense for the restricted ordinary shares based on the grant date fair value. The Company recorded an expense of $260 and $332 for the years ended December 31, 2019 and 2018, respectively. There was no unamortized compensation expense related to restricted ordinary shares as of December 31, 2020 or December 31, 2019. Total unamortized compensation expense related to restricted ordinary shares was $260 as of December 31, 2018 and was recognized over a weighted average period of 0.79 years.

Share Options

Unless specified otherwise in an individual option agreement, share options granted under the 2015 Plan and the 2018 Plan generally have a ten year term and a four year vesting period. The vesting requirement is conditioned upon a grantee's continued service with the Company during the vesting period. Once vested, all awards are exercisable from the date of grant until they expire. The option grants are non-transferable. Vested options generally remain exercisable for 90 days subsequent to the termination of the option holder's service with the Company. In the event of an option holder's disability or death while employed by or providing service to the Company, the exercisable period extends to twelve months or eighteen months, respectively.

The fair value of options granted during the years ended December 31, 2020, 2019 and 2018 was estimated using the Black-Scholes option-pricing model. The inputs for the Black-Scholes model require management's significant assumptions. The risk-free interest rate was based on a normalized estimate of the 7-year U.S. treasury yield. The Company has estimated the expected term utilizing the "simplified" method for awards that qualify as "plain vanilla". The Company does not have sufficient company-specific historical and implied volatility information and it therefore estimates its expected share volatility based on historical volatility information of reasonably comparable guideline public companies and itself. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price. Expected dividend yield is based on the fact that the Company has never paid cash dividends, its ability to pay cash dividends is currently prohibited by the terms of its credit facility with SVB and the Company's future ability to pay cash dividends on its shares may be limited by the terms of any future debt or preferred securities. The Company has elected to account for forfeitures as they occur.

The Company granted 64,840, 512,778 and 479,986 share options to employees and directors during the years ended December 31, 2020, 2019 and 2018, respectively. There were 266,666, 837,386 and 479,986 unvested employee and director options outstanding as of December 31, 2020, December 31, 2019 and December 31, 2018, respectively. Total expense recognized related to the employee and director share options was $1,136, $1,388 and $669 for the years ended December 31, 2020, 2019 and 2018, respectively. Total unamortized compensation expense related to employee and director share options was $970, $3,342 and $2,822 as of December 31, 2020, December 31, 2019 and December 31, 2018, respectively, expected to be recognized over a remaining weighted average vesting period of 1.47 years, 2.61 years and 3.07 years as of December 31, 2020, December 31, 2019 and December 31, 2018, respectively.

The range of assumptions that the Company used to determine the grant date fair value of employee and director options granted were as follows:

	Year ended December 31,		
	2020	2019	2018
Volatility	90.3 - 99.5%	68.9 - 74.5%	60%
Expected term in years	5.50 - 6.25	5.50 - 6.25	6.25
Dividend rate	0%	0%	0%
Risk-free interest rate	0.18 - 0.78%	1.73 - 2.57%	2.16 - 2.91%
Share price	1.68 - 2.03	3.55 - 6.80	7.06 - 13.00
Fair value of option on grant date	1.27 - 1.52	2.37 - 4.41	4.41 - 7.49

The following table summarizes the number of options outstanding and the weighted-average exercise price:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value (in thousands)
Options outstanding December 31, 2017	248,128	$ 3.31	9.44	—
Granted	479,986	$ 12.60		
Exercised	(2,008)	$ 3.30		
Forfeited	(60,887)	$ 10.99		
Options outstanding December 31, 2018	665,219	$ 9.31	8.93	395
Granted	512,778	$ 5.94		
Exercised	(18,232)	$ 3.29		
Forfeited	(8,726)	$ 7.43		
Expired	(769)	$ 6.77		
Options outstanding December 31, 2019	1,150,270	$ 7.92	8.59	254
Granted	64,840	$ 1.69		
Exercised	—			
Forfeited	(134,004)	$ 8.54		
Expired	(127,729)	$ 8.25		
Options outstanding December 31, 2020	953,377	$ 7.36	5.41	—
Exercisable at December 31, 2020	686,711	$ 7.79		

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, 2020 and December 31, 2019.

The weighted average grant-date fair value per share of share options granted during the years ended December 31, 2020, 2019 and 2018 was $1.28, $3.80 and $7.25, respectively.

Restricted Share Units (RSUs)

No RSUs were granted to directors during the year ended December 31, 2020. The Company granted 31,367 and 36,924 RSUs to directors during the years ended December 31, 2019 and 2018, respectively.

(In thousands, except share and per share data)

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

	Number of Shares	Weighted Average Grant Date Fair Value per Share
RSUs outstanding December 31, 2017	—	
Granted	36,924	$ 13.00
Shares vested	—	
Forfeited	—	
RSUs outstanding December 31, 2018	36,924	$ 13.00
Granted	31,367	$ 7.01
Shares vested	(36,924)	$ 13.00
Forfeited	—	
RSUs outstanding December 31, 2019	31,367	$ 7.01
Granted	—	
Shares vested	(25,664)	$ 7.01
Forfeited	(5,703)	$ 7.01
RSUs outstanding December 31, 2020	—	

The fair value of the RSUs is determined on the date of grant based on the market price of the Company's ordinary shares on that date. The fair value of RSUs is expensed ratably over the vesting period, which is generally one year for directors. Total expense recognized related to the RSUs was $63 and $313 for the years ended December 31, 2020 and 2019, respectively. There was no unamortized compensation expense related to the RSUs as of December 31, 2020. Total unamortized compensation expense related to the RSUs was $99 as of December 31, 2019, expected to be recognized over a remaining average vesting period of 0.45 years as of December 31, 2019.

The Company awarded 1,079,000 and 50,000 RSUs to certain employees during the years ended December 31, 2020 and 2019, respectively, which are subject to certain vesting conditions (Performance RSUs). No Performance RSUs were awarded prior to the year ended December 31, 2018.

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

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Performance RSUs outstanding December 31, 2018	—	
Granted	50,000	$8.21
Shares vested	—	
Forfeited	—	
Performance RSUs outstanding December 31, 2019	50,000	$8.21
Granted	1,079,000	$2.04
Shares vested	—	
Forfeited	(146,000)	$3.05
Performance RSUs outstanding December 31, 2020	983,000	$1.99

The weighted average grant date fair value of Performance RSUs with a market condition was determined using the Monte Carlo simulation model. The fair value of Performance RSUs is expensed ratably over the vesting period. Total expense recognized related to the Performance RSUs was $1,560 and $212 for the years ended December 31, 2020 and 2019, respectively. Total unamortized compensation expenses related to Performance RSUs was $152 and $198 for the years ended December 31, 2020 and 2019, respectively, expected to be recognized over a remaining average vesting period of 0.20 years and 0.81 years as of December 31, 2020 and 2019, respectively.

(In thousands, except share and per share data)

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

	Year ended December 31,		
	2020	2019	2018
Research and development expense	$ 754	$ 723	$ 398
General and administrative expense	2,005	1,450	892

There was a total of $1,122, $3,639 and $3,273 unamortized share-based compensation expense for restricted ordinary shares, options, restricted share units and performance restricted share units as of December 31, 2020, December 31, 2019 and December 31, 2018, respectively, expected to be recognized over a remaining average vesting period of 0.80 years, 2.44 years and 2.71 years as of December 31, 2020, December 31, 2019 and December 31, 2018, respectively.

(12) Income Taxes

During the years ended December 31, 2020, 2019 and 2018, 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,		
	2020	2019	2018
Current			
U.S.	$ 743	$ 444	$ 472
Ireland	—	—	—
Total Current	$ 743	$ 444	$ 472
Deferred			
U.S.	$ —	$ —	$ —
Ireland	—	—	—
Total Deferred	$ —	$ —	$ —
Income Tax Provision	$ 743	$ 444	$ 472

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

	Year ended December 31,		
	2020	2019	2018
U.S.	$696	$484	$532
Ireland	(51,959)	(103,170)	(77,116)
Total	$(51,263)	$(102,686)	$(76,584)

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

	Year ended December 31, 2020		Year ended December 31, 2019		Year ended December 31, 2018	
Statutory rate	12.50%	$(6,408)	12.50%	$(12,836)	12.50%	$(9,573)
Impact of U.S. tax rate	(0.20)%	105	(0.07)%	72	(0.11)%	81
Impact of valuation allowance	(6.47)%	3,319	(12.91)%	13,258	(11.42)%	8,749
Research and development tax credit	0.14%	(71)	0.23%	(232)	0.45%	(341)
Adjustments for current tax of prior periods	(1.94)%	995	(0.24)%	241	0.00%	—
Fair value movements on derivative financial instruments	(4.34)%	2,227	0.00%	—	0.00%	—
Other, net	(1.13)%	577	0.06%	(59)	(2.03)%	1,557
Effective tax rate	(1.44)%	$743	(0.43)%	$444	(0.61)%	$472

(In thousands, except share and per share data)

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

	Year ended December 31,		
	2020	2019	2018
Deferred tax assets			
Share-based compensation	$ 650	$ 679	$ 27
Depreciation	31	(24)	(49)
Net operating loss carryforwards	30,261	26,195	13,648
163(j) interest expense limitation	—	730	115
Other	41	84	665
Valuation allowance	(30,983)	(27,664)	(14,406)
Total deferred tax assets	$ —	$ —	$ —
Deferred tax liabilities			
	—	—	—
Total deferred tax assets	$ —	$ —	$ —
Net deferred tax asset	$ —	$ —	$ —

As a Company incorporated in Ireland, it is principally subject to taxation in Ireland.

The Company has net operating loss carryforwards in Ireland of approximately $30,261, $26,195 and $13,648 as of the years ended December 31, 2020, 2019 and 2018, respectively, for which a full valuation allowance has been recognized as it was determined that it is more-likely-than-not that these net deferred tax assets will not be realized. The net operating loss carryforwards do not expire, but are carried forward indefinitely. Realization of these deferred tax assets is dependent on the generation of sufficient taxable income. If the Company demonstrates consistent profitability in the future, the evaluation of the recoverability of these deferred tax assets may change and the remaining valuation allowance may be released in part or in whole. While management expects to realize the deferred tax assets, net of valuation allowances, changes in estimates of future taxable income or in tax laws may alter this expectation.

On December 22, 2017, the United States federal government enacted the Tax Act, marking a change from a worldwide tax system to a modified territorial tax system in the United States. As part of this change, the Tax Act, among other changes, provided a reduction of the U.S. federal corporate income tax rate from 34% to 21%, an indefinite carryforward of net operating losses incurred in 2018 and future periods, and an interest limitation starting in 2018 with an indefinite carryforward. Any impact to the Company related to these items were accounted for in the 2018, 2019 and 2020 tax provisions with minimal impact.

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

	2020	2019
Balance at January 1	$ 2,461	$ 428
Additions	563	2,033
Balance at December 31	$ 3,024	$ 2,461

The Company is generally subject to examination in the Company's primary tax jurisdictions for tax years beginning 2015. The Company is not currently subject to any audits or examination.

(13) 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

(In thousands, except share and per share data)

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.

Contingencies

Liabilities for loss contingencies arising from claims, assessments, litigation, fines, penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. At each reporting date the Company evaluates whether or not a potential loss amount or a potential loss range is probable and reasonably estimable under the provisions of the authoritative guidelines that address accounting for contingencies. The Company expenses costs as incurred in relation to such legal proceedings. The Company is not currently involved in any legal matters.

Under the terms of their respective employment agreements, each of the named executive officers is eligible to receive severance payments and benefits upon a termination without "cause" or due to "permanent disability", or upon "resignation for good reason", contingent upon the named executive officer's continued performance for the Company.

(14) Quarterly Financial Data (unaudited)

	Three months ended			
	December 31, 2020	September 30, 2020	June 30, 2020	March 31, 2020
Revenue	$ —	$ —	$ —	$ —
Total operating expenses	(4,644)	(6,335)	(8,253)	(12,894)
Net loss and comprehensive loss	(11,186)	(12,199)	(12,521)	(16,100)
Net loss attributable to ordinary shareholders	(11,186)	(12,199)	(12,521)	(16,100)
Net loss per share attributable to ordinary shareholders – basic and diluted	$ (0.28)	$ (0.60)	$ (0.80)	$ (1.08)
Weighted average ordinary shares outstanding – basic and diluted	40,645,864	20,392,357	15,614,767	14,868,973

(In thousands, except share and per share data)

	Three months ended			
	December 31, 2019	September 30, 2019	June 30, 2019	March 31, 2019
Revenue	$ —	$ —	$ —	$ 37
Total operating expenses	(23,178)	(30,999)	(27,378)	(20,503)
Net loss and comprehensive loss	(23,641)	(31,271)	(27,638)	(20,580)
Net loss attributable to ordinary shareholders	(23,641)	(31,271)	(27,638)	(20,580)
Net loss per share attributable to ordinary shareholders – basic and diluted	$ (1.59)	$ (2.15)	$ (1.93)	$ (1.44)
Weighted average ordinary shares outstanding – basic and diluted	14,866,838	14,571,278	14,340,231	14,290,437

(15) 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 approximately $51.6 million aggregate principal amount of Exchangeable Notes and $0.1 million aggregate principal amount of RLNs to a group of accredited investors. On September 8, 2020, the Company completed a Rights Offering pursuant to which Iterum Bermuda issued and sold approximately $0.2 million aggregate principal amount of Exchangeable Notes and $0.02 million 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 issued by Iterum Bermuda, which was formed on November 6, 2019 and is a 100% owned "finance subsidiary" of the Company under Rule 13-01 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 ENs 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.

(16) Subsequent Events

On January 28, 2021, at an extraordinary general meeting of shareholders, the Company's shareholders approved an increase of an additional 150,000,000 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 300,000,000 ordinary shares of $0.01 par value each as of March 12, 2021. The holders of ordinary shares are entitled to one vote for each share held. The holders of ordinary shares have no preemptive or other subscription rights, and there are no redemption or sinking fund provisions with respect to such shares.

On February 3, 2021, the Company entered into an amended and restated underwriting agreement (the Underwriting Agreement) to issue and sell 34,782,609 ordinary shares of the Company, $0.01 nominal value per share, in a firm commitment underwritten public offering with a public offering price of $1.15 per share (the February Underwritten Offering). The Company offered the ordinary shares in the February Underwritten Offering pursuant to its universal shelf registration statement on Form S-3. The February 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 5,217,391 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 40,000,000 shares, which resulted in aggregate net proceeds of approximately $42,096 after deducting underwriting discounts and commissions and estimated offering expenses. In addition, pursuant to the Underwriting Agreement, the Company agreed to issue to the underwriter's designees warrants to purchase 2,800,000 ordinary shares, which was equal to 7.0% of the aggregate number of ordinary shares sold in the February Underwritten Offering. The warrants issued to such designees have an exercise price of $1.4375 per ordinary share, were exercisable upon issuance and will expire on February 3, 2026.

On February 9, 2021, the Company entered into a securities purchase agreement (the February SPA) with several healthcare-focused institutional investors pursuant to which the Company agreed to issue and sell in a registered direct offering (the February Registered Direct Offering) an aggregate of 17,500,000 ordinary shares, $0.01 nominal value per share, at a purchase price of $2.00 per share, for aggregate net proceeds to the Company of approximately $32,200 after deducting placement agent fees and other estimated offering expenses. The Company offered the ordinary shares in the February Registered Direct Offering pursuant to its universal shelf registration statement on Form S-3. The February Registered Direct Offering closed on February 12, 2021. Warrants to purchase 1,225,000 ordinary shares, which was equal 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 Registered Direct Offering. Upon closing, warrants issued to such designees became exercisable immediately at an exercise price of $2.50 per ordinary share, subject to adjustment in certain circumstances, and will expire on February 9, 2026.

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, 2020. 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, 2020, 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, 2020.

Our independent registered public accounting firm has not performed an evaluation of our internal control over financial reporting during any period in accordance with the provisions of the Sarbanes-Oxley Act. For as long as we remain an "emerging growth company" as defined in Rule 12b-2 of the Exchange Act, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the year ended December 31, 2020, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is incorporated herein by reference to our definitive Proxy Statement to be filed in connection with our 2021 Annual General Meeting of Shareholders, or our 2021 Proxy Statement, which will be filed with the Securities and Exchange Commission within 120 days after December 31, 2020.

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 2021 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 2021 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 2021 Proxy Statement.

I tem 14. Principal Accounting Fees and Services.

The information required by this item is incorporated herein by reference to our 2021 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)	January 28, 2021	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	X			
3.5	Amended and Restated Certificate of Incorporation of Iterum Therapeutics US Limited	X			
3.6	Bylaws of Iterum Therapeutics US Limited	X			
3.7	Certificate of Amendement of Certificate of Incorporation of Iterum Therapeutics US Holding Limited	X			
3.8	Bylaws of Iterum Therapeutics US Holding Limited	X			
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

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
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 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.		Form S-1 (Exhibit 10.3)	May 1, 2018	333-224582
10.4	Forms of U.S. Stock Option Agreement, Stock Option Grant Notice and Notice of Exercise under the 2015 Equity Incentive Plan.		Form S-1 (Exhibit 10.4)	May 1, 2018	333-224582
10.5	Forms of Irish Stock Option Agreement, Stock Option Grant Notice and Notice of Exercise under the 2015 Equity Incentive Plan.		Form S-1 (Exhibit 10.5)	May 1, 2018	333-224582
10.6	Amended and Restated 2018 Equity Incentive Plan		Form 8-K (Exhibit 99.1)	June 15, 2020	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

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
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+	Non-Employee Director Compensation Policy.		Form S-1/A (Exhibit 10.18)	May 16, 2018	333-224582
10.18	Loan and Security Agreement by and among Silicon Valley Bank, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited, and Iterum Therapeutics US Limited, dated April 27, 2018.		Form S-1/A (Exhibit 10.19)	May 4, 2018	333-224582
10.19	Intellectual Property Security Agreement by and among Silicon Valley Bank, the Registrant, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited, and Iterum Therapeutics US Limited, dated April 27, 2018.		Form S-1/A (Exhibit 10.20)	May 4, 2018	333-224582
10.20	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
10.21	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
10.22	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
10.23	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
10.24	First Amendment to Loan and Security Agreement, dated as of January 16, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and Silicon Valley Bank.		Form 8-K (Exhibit 10.3)	January 17, 2020	001-38503
10.25	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
10.26	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
10.27	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
10.28	Securities Purchase Agreement, dated as of February 9, 2021, by and among Iterum Therapeutics plc and the purchasers party thereto	X			

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
21.1	Subsidiaries of the Registrant.		Form 10-K (Exhibit 21.1)	March 12, 2020	001-38503
22.1	Subsidiary Guarantors and Subsidiary Issuers	X			
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			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X			

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+ Indicates management contract or compensatory plan.

† Confidential treatment has been granted for certain provisions omitted from this Exhibit pursuant to Rule 406 promulgated under the Securities Act. The omitted information has been filed separately with the Securities and Exchange Commission.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

ITERUM THERAPEUTICS PLC

Date: March 12, 2021

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

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

SIGNATURE	TITLE	DATE
/s/ Corey N. Fishman Corey N. Fishman	President and Chief Executive Officer (Principal Executive Officer)	March 12, 2021
/s/ Judith M. Matthews Judith M. Matthews	Chief Financial Officer (Principal Financial and Accounting Officer)	March 12, 2021
/s/ Brenton K. Ahrens Brenton K. Ahrens	Director	March 12, 2021
/s/ Mark Chin Mark Chin	Director	March 12, 2021
/s/ Michael Dunne Michael Dunne M.D.	Director	March 12, 2021
/s/ Patrick J. Heron Patrick J. Heron	Director	March 12, 2021
/s/ Ronald M. Hunt Ronald M. Hunt	Director	March 12, 2021
/s/ David G. Kelly David G. Kelly	Director	March 12, 2021
/s/ Shahzad Malik Shahzad Malik, M.D.	Director	March 12, 2021

COMPANIES ACT 2014

PRIVATE COMPANY LIMITED BY SHARES

CONSTITUTION

OF

ITERUM THERAPEUTICS INTERNATIONAL LIMITED

(as amended by special resolution dated 13 June 2018)

COMPANIES ACT 2014

PRIVATE COMPANY LIMITED BY SHARES

CONSTITUTION

OF

ITERUM THERAPEUTICS INTERNATIONAL LIMITED

1. **Company Name:** The name of the company is: ITERUM THERAPEUTICS INTERNATIONAL LIMITED.

2. **Company Type:** The company is a private company limited by shares, registered under Part 2 of the Companies Act 2014.

3. **Liability of Members:** The liability of the members is limited.

4. **Share Capital:**

The share capital of the company is divided into shares of €1 and $0.0001 each.

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

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

Act means the Companies Act 2014;

committee means a committee established by the directors which may consist in whole or in part of members of the board of directors of the company;

director means a director for the time being of the company or a director present at a meeting of the board of directors and includes any person occupying the position of director by whatever name called, and **directors** means all of such persons;

the seal means the common seal of the company;

the register means the register of members to be kept as required by the Act and **registered address** means the address of a member as entered in the register;

Ireland means Ireland excluding Northern Ireland;

5.2. The provisions of the Act which are stated therein to apply to a private company limited by shares, save to the extent that its constitution is permitted to provide or state otherwise, will apply to the company subject to the alterations, modifications and exclusions contained in this Constitution, and will, so far as not inconsistent with this Constitution, bind the company and the members.

5.3. Unless the contrary is clearly stated, references to the Act or to any other enactment (including any subordinate legislation) or any section or provision thereof shall mean the Act or such enactment, subordinate legislation, section or provision (as the case may be), as the same may be consolidated, amended, extended, modified, supplemented or re-enacted (whether before or after the date hereof) from time to time and may be for the time being in force.

5.4. Unless specifically defined in this Constitution or the context otherwise requires, words or expressions contained in th is Constitution and not specifically defined herein shall bear the same meaning s as in the Act , but excluding any statutory modification thereof not in force when th is Constitution became binding on the company and the members.

5.5. Reference to any document includes that document as amended or supplemented from time to time.

5.6. Unless the context otherwise requires, expressions in this Constitution referring to writing shall be construed, unless the contrary intention appears, as including references to printing, lithography, photography and to writing in electronic form and any other modes of representing or reproducing words in a visible form, and expressions in this Constitution referring to execution of any document shall include any mode of execution whether under seal or under hand.

5.7. Unless otherwise specifically provided in this Constitution, references in this Constitution to the directors of the company shall, where the company has a sole director, be read as references to the director of the company, references in this Constitution to the board of directors of a company shall, where the company has a sole director, be read as references to the director of the company, and references to the opinion, discretion or powers of the directors shall, where the company has a sole director, be read as references to the opinion, discretion or powers of that director.

5.8. Unless the context otherwise requires, words importing the singular include the plural and vice versa, words importing the masculine include the feminine, and words importing persons include corporations.

5.9. Headings are inserted for convenience only and do not affect the construction or interpretation of this Constitution.

5.10. Unless the context otherwise requires, reference to Regulations and to paragraphs in this Constitution are to the Regulations, and paragraphs of the Regulations, of this Constitution.

6. **Company Seal:** Without prejudice to the provisions of the Act in relation to the use of the seal of a company, any registered person authorised by the board of directors of the company in accordance with the applicable provisions of the Act will be entitled to use the seal of the company and may sign or countersign an instrument to which the seal is affixed, and an alternate who is not also a director will also be entitled to sign or countersign an instrument to which the seal is affixed, as if he were the director who appointed him.

7. **Official Seal:** The company may have for use in any place abroad an official seal which shall resemble the seal of the company with the addition on its face of the name of every place abroad where it is to be used.

8. **Authority to Allot Shares:**

8.1. The allotment of shares is hereby generally and unconditionally authorised without any limit or restriction as to the number or amount of shares that may be allotted or the period of time during which they may be allotted.

8.2. Section 69(6) of the Act is hereby excluded in relation to all allotments of shares by the company.

8.3. Shares and any other securities of the company may only be allotted by the directors or a duly authorised committee thereof and the directors (or any duly authorised committee) may allot, grant options over, issue or otherwise dispose of shares or other securities to such persons, on such terms and conditions, and at such times as they may determine in their absolute discretion.

8.4. The directors or any duly authorised committee thereof may execute and do all such documents, acts and things as in their opinion are necessary or desirable in order to give effect to the authority conferred by this Regulation.

8.5. For the purposes of this Regulation, **shares** includes a right to subscribe for shares or to convert securities into shares and **securities** has the meaning given to such term in Section 64(1) of the Act.

9. **Lien**

9.1. The Company's first and paramount lien on every share called or payable at a fixed time in respect of that share and the extension of that lien to all dividends payable thereon shall not apply where any such shares have been mortgaged or charged by way of security in which event such lien shall rank behind any such security and section 80(2)-(4) of the Act shall be modified accordingly.

10. **Transfer of Shares:**

10.1. The instrument of transfer of any share shall be executed by or on behalf of the transferor, save that if the share concerned (or one or more of the shares concerned) is not fully paid, the instrument shall be executed by or on behalf of the transferor and the transferee.

10.2. The foregoing paragraph 10.1 is subject in its entirety to paragraph 10.3 of this Regulation.

10.3. Notwithstanding anything to the contrary contained in these Regulations, the directors shall promptly register any transfer of shares and shall not suspend registration thereof where such transfer:-

10.3.1. is to any bank or institution or to any third party to whom such shares have been charged by way of security or to any nominee or any transferee of such bank or institution or third party (a **Secured Institution**); or

10.3.2. is delivered to the company for registration by a Secured Institution or its nominee in order to register the Secured Institution as legal owner of the shares (a **Transfer relating to Share Security**); or

10.3.3. is executed by a Secured Institution or its nominee pursuant to the power of sale or other power under such security, and furthermore, notwithstanding anything to the contrary contained in these Regulations or in any agreement or arrangement applicable to any shares in the Company, no transferor or proposed transferor of any such shares to a Secured Institution or its nominee and no Secured Institution or its nominee (each a **Relevant Person**), shall be required to obtain the approval of the directors or be subject to, or obliged to comply with, any rights of pre-emption contained in these Regulations or any such agreement or arrangement nor shall any Relevant Person be otherwise required to offer the shares which are or are to be the subject of any transfer as aforesaid to the shareholders for the time being of the Company or any of them, and no such shareholder shall have any right under the Regulations or otherwise howsoever to require such shares to be transferred to them whether for consideration or not. No resolution shall be proposed or passed the effect of which would be to delete or amend this Regulation unless not less than 45 days' written notice thereof shall have been given to any such Secured Institution by the Company, which notice must be sent by pre-paid registered post to its registered office or principal place of business in the State marked for the attention of the company secretary and Section 95(1)(a) of the Act shall be modified accordingly.

11. **Transmission of Shares by Operation of Law in Consequence of a Merger:**

11.1. In any case in which any share or shares in the company (**Relevant Shares**) which are held by another company or body corporate, wherever incorporated (the **Corporate Member**) is or are transmitted by operation of law in consequence of a merger involving the Corporate Member and one or more other companies (which may include the company) or bodies corporate, wherever incorporated, and which is put into effect in accordance with the provisions in that regard contained in the Act, in the European Communities (Cross-Border Mergers) Regulations 2008 (S.I. No. 157 of 2008) (as amended), or in any other applicable law or other enactment (a **merger**) and if, in any such case, the provisions of Section 480(6) of the Act are not applicable for any reason, a transfer of the Relevant Shares may be validly effected in accordance with the following provisions of this Regulation.

11.2. In any case as is menti oned in the foregoing paragraph 11.1 of this Regulation, any person who is or who becomes entitled to any Relevant Shares in consequence of any such merger (a **Relevant Person**) may, subject always to paragraph 1 1.3 of this Regulation, upon such evidence being produced as may from time to time be required by the directors of the company (including without limitation any information and documentation relating to the merger and the title and other rights of the Relevant Person to the Relevant Shares arising as a result thereof) elect either to be registered himself in the register as holder of the Relevant Shares, or, to the extent permitted by law, to have some person nominated by him (being a person who consents to be so registered) registered in the register as the transferee thereof.

11.3. The directors of the company shall, in either of those cases, have the same rights under the Act or this Constitution to decline or suspend registration as they would have had in the case of a transfer of the Relevant Shares by the Corporate Member before the merger was put into effect as aforesaid.

11.4. If the Relevant Person elects to be so registered himself, the Relevant Person shall furnish to the company a notice in writing signed by him stating that he so elects, and if the Relevant Person elects, to the extent permitted by law, to have another person registered instead, the Relevant Person shall testify his or her election by executing in favour of that other person a transfer of the Relevant Shares.

11.5. All the limitations, restrictions and provisions contained in the Act or in this Constitution relating to the right to transfer and the registration of a transfer of a share shall be applicable to a notice or transfer referred to in paragraph 11.4 of this Regulation as if the merger had not occurred and the notice or transfer were a transfer signed by the Corporate Member.

11.6. Subject to paragraph 11.7 of this Regulation, the Relevant Person (or any other person nominated by him, to the extent permitted by law, in accordance with the foregoing provisions of this Regulation) shall, on and from the effective date of the merger, be entitled to the same dividends, bonus and other monies payable in respect of the Relevant Shares and other advantages to which he would be entitled if he was the registered holder of the Relevant Shares but shall not, before being registered in the register as a member in respect of the Relevant Shares, be entitled in respect of them to exercise any rights conferred by membership in relation to meetings of the company.

11.7. The directors of the company may at any time serve a notice on any Relevant Person requiring the Relevant Person to make the election, to the extent permitted by law, provided for by paragraph 11.2 of this Regulation and, if the person does not make that election (and proceed to do, consequent on that election, whichever of the things mentioned in paragraph 11.4 of this Regulation is appropriate) within 90 days after the service of the notice, the directors may thereupon withhold payment of all dividends, bonuses or other monies payable in respect of the Relevant Shares until the requirements of the notice have been complied with.

11.8. The company may charge a fee not exceeding €10 on the registration of any person entitled to a share in consequence of a merger in accordance with the foregoing provisions of this Regulation.

11.9. The provisions of this Regulation shall be subject to any order made by a court having lawful jurisdiction in respect of a merger.

12. **Acquisition of Own Shares:** Subject to (and without prejudice to) the provisions of the Act, the company may acquire its own shares by purchase, or in the case of redeemable shares, by redemption or purchase, on such terms (including as to the consideration for, and the timing of, any such purchase or redemption) and in such a manner as shall be determined by the directors in their absolute discretion.

13. **Number of Directors:** The company shall have at least one director. No director who has been appointed by the directors, as permitted by the Act, will require to be re-elected at the next following annual general meeting or at any extraordinary general meeting following such appointment.

14. **Committees of Directors:** The meetings and proceedings of any committee formed by the directors will be governed by the provisions set out in the Act regulating the meetings and proceedings of directors so far as the same are applicable and are not superseded by any regulations imposed on such committee by the directors from time to time.

15. **Vacation of Office of Director:**

15.1. The office of a director shall, in addition to the circumstances in which it shall be vacated described in Section 136 (*share qualification, if applicable*) and Section 148(1) (*bankruptcy and disqualification*), also be vacated automatically if the director dies in office, or if the director:

15.1.1. becomes subject to a declaration of restriction made pursuant to Chapter 3 of Part 14 of the Act; or

15.1.2. is sentenced to a term of imprisonment following conviction of any indictable offence, unless the term of imprisonment is suspended, such that he is not imprisoned in respect of the offence; or

15.1.3. is absent for more than six consecutive months without the permission of the directors from meetings of the directors or any committee thereof held during that period and his alternate director (if any) shall not have attended any such meetings in his place during such period, and his co-directors resolve that, by reason of such absence, he has vacated his office; or

15.1.4. is removed from office by notice in writing served upon him signed by all his co-directors (any such removal being deemed to be an act of the company); or

15.1.5. is no longer reasonably regarded by his co-directors as possessing an adequate decision-making capacity for reasons of health, and his co-directors have accordingly resolved that his office be vacated on this ground, or he becomes the subject of an order made in Ireland or elsewhere by a court claiming jurisdiction in that regard for his detention or for the appointment of a guardian or other person to exercise powers with respect to his property or affairs, on the ground, in any such case, of mental disorder or incapacity;

15.1.6. resigns his office by notice in writing to the company; or

15.1.7. makes any arrangement or composition in Ireland or elsewhere with his creditors generally, and his co-directors resolve, for that reason, that his office be vacated.

15.2. The provisions of paragraphs 15.1.1 to 15.1.7 of this Regulation shall apply to the exclusion of the provisions of Section 148(2) of the Act.

16. **Alternate Directors:**

16.1. Any director (the **appointer**) may at any time and from time to time appoint by notice in writing to the company any person to be his alternate.

16.2. A person may act as an alternate for more than one director and while he is so acting will be entitled to a separate vote for each director he is representing and, if he is himself a director, his vote or votes as an alternate will be in addition to his own vote.

16.3. An alternate will be counted for the purpose of reckoning whether a quorum is present at any meeting attended by him at which he is entitled to vote, but where he is himself a director or is the alternate of more than one director he will only be counted once for such purpose.

16.4. An alternate will be entitled, subject to his giving to the company an address to receive notice of all meetings of the directors and of all meetings of committees of which his appointer is a member, to receive notice of and attend and vote at any meeting of the directors (or of a committee of which his appointer is a member) at which the appointer is not personally present. An alternate shall not be entitled to be remunerated or paid fees otherwise than out of the remuneration or fees as the case may be paid to the appointer.

16.5. The alternate will be entitled, in the absence of the appointer, to exercise all the powers, rights, duties and authorities of the appointer as a director (other than the right to appoint an alternate hereunder).

16.6. An alternate's appointment will automatically come to an end if for any reason the appointer ceases to be a director, but if a director retires but is re-appointed or deemed to have been re-appointed at the meeting at which he retires, any appointment of an alternate made by him which was in force immediately prior to his retirement will continue after his re-appointment. Section 165(5) and (6) of the Act in relation to revocation of appointment shall apply.

17. **Managing and Executive Directors:**

17.1. Subject to the other provisions of this Constitution, the directors may from time to time appoint one or more of themselves to be managing director or chief executive officer or any other category of executive director (by whatever name called) for such period, and on such terms as to remuneration or otherwise, as they think fit and, subject to the terms of any agreement entered into in any particular case, may revoke such appointment. The directors may entrust to and confer upon any director so appointed any of the powers exercisable by them upon such terms and conditions and with such restrictions (if any) as they may think fit, and either concurrently with or to the exclusion of their own powers, and may from time to time revoke, withdraw, alter or vary all or any conferral of such powers. Section 159(2) of the Act shall not apply in relation to any such appointment.

18. **Directors' Contracts:**

18.1. Notwithstanding the provisions of Section 162 of the Act, no contract will be entered into by the company for the employment of, or the provision of services by, a director or a director of a holding company of the company containing a term to which Section 249 of the Act applies, without obtaining the approval provided for in that Section.

19. **Directors' Right to Attend Meetings:**

19.1. A director who is not a member of the company will nevertheless be entitled to receive notice of, attend and speak at any general meeting or separate meeting of the holders of any class of share.

20. **Voting by Directors:**

20.1. A director may vote in respect of any contract, appointment or arrangement in which he is interested, and he shall be counted in the quorum present at any meeting at which such matters are considered. Section 163 of the Act shall not apply.

21. **Remuneration of Directors:**

21.1. The remuneration which shall include benefits in kind, and any fees, to be paid to directors of the company shall be at such rate and basis as the directors shall determine from time to time. The directors shall also be entitled to be paid their travelling, hotel and other expenses properly incurred by them in attending and returning from meetings of the directors or any committee of the directors or general meetings of the company or otherwise in connection with the business of the company, or to receive a fixed allowance in respect thereof as may be determined by the directors from time to time, or a combination partly of one such method and partly of the other. The amount, rate or basis of the fees, remuneration or expenses paid or to be paid to the directors shall not require the approval of or ratification by the company in general meeting.

21.2. The board may approve additional remuneration to any director undertaking any special work or services for, or undertaking any special task on behalf of the company including participating as a member of a committee, in addition to his ordinary work as a director. Any remuneration or fees paid by a director who is also a legal adviser to the company or otherwise serves the company in a professional capacity shall be in addition to any remuneration or fees paid to him as a director of the company.

22. **Resolutions in Writing:**

22.1. Notwithstanding the provisions of Section 161(1) of the Act, a resolution in writing signed by each director or by his alternate will be as valid as if it had been passed at a meeting of the directors duly convened and held.

22.2. A resolution in writing signed by each member of a committee (or, in the case of a director, his alternate) will be as valid as if it had been passed at a meeting of that committee duly convened and held.

22.3. Any such resolution as is referred to in this Regulation may consist of one document or two or more documents in like form to the same effect, each signed by one or more of the signatories, and for all purposes shall take effect from the time that it is signed by the last such signatory.

23. **Certain matters not to amount to conflicts of interest, etc.:**

23.1. A director who has been validly appointed or nominated for appointment by a particular member or members may (i) be a director or other officer of, employed by or otherwise interested (including by the holding of shares) in, any such member or members, or of any body corporate owned or controlled by any such member or members, and (ii) have regard to the interests of that member or members, and shall not be deemed to have a conflict of interest or to be in breach of his duty under Section 228(1)(f) of the Act in any such circumstances.

23.2. A director who declares the nature of his interest in a contract (as the expression **contract** is to be interpreted by Section 231 of the Act) or proposed contract with the company in accordance with the requirements of the Act in that regard shall not be deemed to be in breach of his duty under Section 228(1)(f) of the Act, but this is without prejudice to the powers of the directors to take any action which they may consider appropriate in their discretion in relation to any matters so disclosed.

24. **Use of company property:**

24.1. Unless the members of the company in general meeting shall otherwise determine, and subject always to the other Regulations of this Constitution, any director may use, for his own benefit, any of the company's property where the other directors or the members of the company have given their consent (whether express or implied) to that use.

25. **Proxies:**

25.1. The instrument appointing a proxy shall be in the form prescribed by the Act, or as near to it as circumstances permit. The instrument of proxy and the power of attorney or other authority, if any, under which it is signed, or a notarially certified copy of that power or authority, shall be deposited at the registered office of the company or at such other place within Ireland as is specified for that purpose in the notice convening the meeting of the company, and shall be so deposited not later than before the commencement of the meeting or adjourned meeting at which the person named in the instrument proposes to vote or, in the case of a poll, before the commencement of the taking of the poll.

25.2. The directors or the secretary may from time to time permit appointments of a proxy to be made by means of an electronic or internet communication or facility or by facsimile transmission, and may permit supplements, amendments or revocations of any such appointments to be made by similar means. Any such appointments of proxy and any such supplements, amendments or revocations thereof may be made subject to such terms and conditions as the directors or secretary may determine from time to time in their or his discretion, and any such appointments, supplements, amendments or revocations of proxy will be deemed deposited at the place specified for such purpose, once received by the company. The directors may treat any such communication, facility or transmission which purports to be or is expressed to be sent on behalf of a member as sufficient evidence of the authority of the person sending it to send it on behalf of that member.

26. **Business of AGM:** Without prejudice to the powers of the directors to include on the agenda of any annual general meeting of the company such other matters as they may, in their absolute discretion, think fit, the business of the annual general meeting of the company shall be required to include only the following matters:

26.1. the consideration of the company’s statutory financial statements and the report of the directors and, unless the company is entitled to and has availed itself of the audit exemption under Section 360 or Section 365 of the Act, the report of the statutory auditors on those statements and that report;

26.2. the review by the members of the company’s affairs; and

26.3. save where the company is entitled to and has availed itself of the exemption referred to in paragraph 1 of this Regulation, the appointment or re-appointment of statutory auditors.

27. **General Meetings outside Ireland:** An annual general meeting or an extraordinary general meeting of the company may be held inside or outside Ireland provided that, if the company holds any such meeting outside Ireland then, unless all of the members entitled to attend and vote at such meeting consent in writing to its being held outside Ireland, the company shall at its own expense make all necessary arrangements to ensure that members can, by technological means, participate in any such meeting without leaving Ireland.

28. **General Meetings including Quorum:** The quorum for general meetings of the company shall be two members present in person or by proxy unless the company is a single-member company, in which case one member present in person or by proxy shall be a quorum.

29. **Company may dispense with holding an Annual General Meeting:**

29.1. The company need not hold an annual general meeting in any year where all the members entitled, as at the date of the written resolution referred to in this Regulation, to attend and vote at such general meeting have signed, before the latest date for the holding of the meeting, a written resolution, complying with the provisions of the Act, acknowledging receipt of the financial statements that would have been laid before that meeting, resolving all such matters as would have been resolved at that meeting, and confirming that no change is proposed in the appointment of the person (if any) who, at the date of the resolution, stands appointed as statutory auditor of the company.

30. **Right to demand a poll:**

30.1. At any general meeting a poll may be demanded by:

30.1.1. the chairperson of the meeting;

30.1.2. at least three members present in person or by proxy;

30.1.3. any member or members present in person or by proxy and representing not less than 10 per cent of the total voting rights of all the members of the company having the right to vote at the meeting; or

30.1.4. a member or members holding shares in the company conferring the right to vote at the meeting being shares on which an aggregate sum has been paid up equal to not less than 10 per cent of the total sum paid up on all the shares conferring that right.

31. **Restriction on voting:** For so long as the company holds any shares as treasury shares, or any subsidiary of the company holds shares in the company, then the company or the subsidiary (as the case may be) shall not exercise any voting rights in respect of the shares.

32. **Unanimous Written Resolutions and Majority Written Resolutions**

A unanimous written resolution and a majority written resolution may be passed by members subject to and in accordance with Section 193 and Section 194 respectively of the Act.

33. **Directors' and Officers' Indemnity:** Subject to the provisions of the Act, every director, managing director, chief executive officer, secretary and other officer for the time being of the company shall be indemnified out of the assets of the company against any liability incurred by him:

33.1. in defending any proceedings, whether civil or criminal, in relation to his acts or omissions while acting in such office, in which judgment is given in his favour or in which he is acquitted; or

33.2. in connection with any proceedings or application referred to in, or under, Sections 233 or 234 of the Act in which relief is granted to him by the court.

34. **Notices:**

34.1. Any notice or document to be served on or given to a member of the company by the company or by an officer of the company whether pursuant to any provision of the Act or this Constitution or otherwise may be served on or given to the member in any of the ways specified in subsection (3) of Section 218 of the Act (including by electronic means provided that in such a case the conditions specified in subsection (4) of that Section are satisfied), and the notice or document shall be deemed to have been served or given as follows:-

34.1.1. if given personally or delivered to the member, when so given or delivered;

34.1.2. if left at the registered address of the member, when so left at that address;

34.1.3. if the notice is a notice of a general meeting, and it is posted using ordinary pre-paid post to the registered address of the member, on the expiration of 24 hours following posting (as permitted by Section 181(3) of the Act) but in a case where the notice or document is not a notice of a meeting, it shall be deemed to have been given or served 48 hours after the cover containing it was posted, and if so posted on a Friday, 72 hours after it was so posted; and

34.1.4. if served on or delivered to a member by electronic means, both in the case of the service or giving of the notice or document by sending it by electronic mail and by making it available or displaying it on a website, 12 hours after the time it was sent, or made available or displayed.

34.2. Where the company is required or obliged to serve a notice on or give it to a person other than a member of the company, it shall be in writing and, without prejudice to any method of service provided for in the Act, may be served on or given to that person personally, or by leaving it at or posting it to the last-known postal address of that person, or by sending it to the other person by electronic mail provided that the person has consented to the use of electronic mail to serve or give notices on or to such person and has not, at the time that electronic mail is so used, given written notice to the company in accordance with the provisions of this Constitution withdrawing that consent. A notice or document given or served in a manner referred to in this paragraph shall be deemed to have been given or served as follows:

34.2.1. if given personally, when so given;

34.2.2. if left at the last-known postal address of the person, when so left at that address;

34.2.3. if posted using ordinary pre-paid post to the last-known postal address of the other person on any day other than a Friday, 48 hours after the cover containing it was posted, and if so posted on a Friday, 72 hours after it was so posted; and

34.2.4. if served on or delivered to the other person by electronic mail, 12 hours after the time it was sent.

34.3. Without prejudice to any provision of the Act or of these Regulations concerning the sending of notices or other documents to the company, any notice or other document which is required to be served on or given to the company by a member or by any other person under the Act or this Constitution shall be in writing and in the English language, and may be served on or given to the company by giving or delivering it personally to the secretary of the company or by posting it using ordinary pre-paid post to the registered office of the company marked for the attention of the secretary, and will be deemed to have been served on or given to the company;

34.3.1. if given or delivered personally, when so given or delivered; and

34.3.2. if posted in the manner described in this paragraph on any day other than a Friday, 48 hours after the cover containing it was posted, and if so posted on a Friday, 72 hours after it was so posted.

35. **Single-member Company:**

35.1. If at any time the company has only one member, that is to say that all the issued shares of the company are registered in the name of a sole person (whether a natural person or a body corporate), it will be a single-member company within the meaning of the Act. If and so long as the company is a single-member company, the sole member may appoint a person to be a director of the company by serving a notice in writing on the company which states that the named person is appointed director, and this applies notwithstanding anything in subsection (3) of Section 144 of the Act (save for the requirement of it that any limit for the time being on the number of directors provided for in this Constitution (if any) is to be observed) or in subsection (4) of Section 144.

35.2. Where the company is a single-member company and the sole member takes any decision which has effect, pursuant to Section 196 of the Act, as if agreed by the company in general meeting, the member shall provide the company with a written record of that decision, unless the decision is taken by way of written resolution which the member has already forwarded to the company, and where the company is notified by the sole member of a decision taken by way of a written resolution, or of a written record of a decision taken by that sole member, the company shall record and retain the notification in a book or other suitable means maintained for the purpose.

35.3. Where the company is a single-member company and the sole member exercises or discharges any power, right or obligation pursuant to Section 196 of the Act, involving or consisting of the passing of a resolution, or the sole member agreeing to a thing, and the provisions of Section 198 shall apply to that resolution or thing, the company shall notify such exercise or discharge in writing within 15 days of the occurrence thereof to the Registrar of Companies.

35.4. Where the company is a single-member company and enters into a contract with the sole member which is not in the ordinary course of business and which is not in writing, and the sole member also represents the company in the transaction (whether as a director or otherwise), the company shall ensure that the terms of the contract are forthwith set out in a written memorandum or are recorded in the minutes of the next directors' meeting.

We, the body corporate whose name and address is subscribed, wish to be formed into a company in pursuance of this Constitution, and we agree to take the number of shares in the capital of the company set opposite our name.

Names, Addresses and Descriptions of Subscriber	*Number of Shares taken by the Subscriber*
Iterum Therapeutics Limited, 25/28 North Wall Quay, Dublin 1 Private Company Limited By Shares	1
Total Shares Taken:	1

Signature in writing of the above subscriber, attested by witness as provided for below

_____

For and on behalf of Iterum Therapeutics Limited

Dated 2015

Witness to the above Signature:

Signature: _____

Name: _____

Address: _____

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION OF ITERUM THERAPEUTICS US LIMITED

Judith M. Matthews hereby certifies that:

ONE: The date of filing the original Certificate of Incorporation of this corporation with the Secretary of State of the State of Delaware was October 21, 2015.

TWO: She is the duly elected and acting President of Iterum Therapeutics US Limited, a Delaware corporation.

THREE: The Certificate of Incorporation of this corporation is hereby amended and restated to read as follows:

I.

The name of this corporation is Iterum Therapeutics US Limited (the *"**Company**").*

II.

The registered office of the corporation in the State of Delaware shall be 2711 Centerville Road, Suite 400, City of Wilmington, County of New Castle, 19808 and the name of the registered agent of the corporation in the State of Delaware at such address is Corporation Service Company.

III.

The purpose of this corporation is to engage in any lawful act or activity for which a corporation may be organized under the Delaware General Corporation Law (the *"**DGCL**").*

IV.

This corporation is authorized to issue only one class of stock, to be designated Common Stock. The total number of shares of Common Stock presently authorized is 100, each having a par value of $0.0001.

V.

For so long as any shares of Common Stock remain outstanding, in addition to any other vote or consent required herein or by law, the vote or written consent of the holders of a majority of the outstanding shares of Common Stock shall be necessary for effecting or validating the following actions (whether by merger, recapitalization or otherwise):

1. Any amendment, alteration, or repeal of any provision of the Certificate of Incorporation or Bylaws of the Company;

2. Any increase or decrease in the authorized number of shares of the Company;

3. Any authorization or any designation, whether by reclassification or otherwise or any other action resulting in the creation of any new class or series of shares or any other securities convertible into a new class or series of shares of the Company;

4. Any redemption, repurchase, payment or declaration of dividends or other distributions or return of capital (except for acquisitions of shares by the Company pursuant to agreements that permit the Company to repurchase such shares at no more than cost upon termination of services to the Company);

5. Any agreement by the Company or its stockholders regarding or any other action resulting in an Asset Transfer or Acquisition (as defined below);

6. Any incurrence of bank indebtedness of US$500,000 or more individually or in the aggregate with all other bank indebtedness of the Company (other than payables incurred in the ordinary course of business);

7. Any voluntary dissolution or liquidation of the Company;

8. Any increase or decrease in the authorized number of members of the Company's Board; or

9. Any increase in the number of shares available for issuance under any existing equity incentive plan.

*"**Asset Transfer**"* shall mean a sale, lease, exclusive license, assignment or other disposition of all or substantially all of the business or assets of the Company.

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

VI.

A. The management of the business and the conduct of the affairs of the corporation shall be vested in its Board of Directors. The number of directors which shall constitute the whole Board of Directors shall be fixed by the Board of Directors in the manner provided in the Bylaws.

B. No person entitled to vote at an election for directors may cumulate votes to which such person is entitled unless required by applicable law at the time of such election. During such time or times that applicable law requires cumulative voting, every stockholder entitled to vote at an election for directors may cumulate such stockholder's votes and give one candidate a number of votes equal to the number of directors to be elected multiplied by the number of votes to which such stockholder's shares are otherwise entitled, or distribute the stockholder's votes on the same principle among as many candidates as such stockholder desires. No stockholder, however, shall be entitled to so cumulate such stockholder's votes unless (A) the names of such candidate or candidates have been placed in nomination prior to the voting and (B) the stockholder has given notice at the meeting, prior to the voting, of such stockholder's intention to cumulate such stockholder's votes. If any stockholder has given proper notice to cumulate votes, all stockholders may cumulate their votes for any candidates who have been properly placed in nomination. Under cumulative voting, the candidates receiving the highest number of votes, up to the number of directors to be elected, are elected.

C. The Board of Directors is expressly empowered to adopt, amend or repeal the Bylaws of the corporation. The stockholders shall also have power to adopt, amend or repeal the Bylaws of the corporation; provided, however, that, in addition to any vote of the holders of any class or series of stock of the corporation required by law or by this Restated Certificate, such action by stockholders shall require the affirmative vote of the holders of at least a majority of the voting power of all of the then-outstanding shares of the capital stock of the corporation entitled to vote generally in the election of directors, voting together as a single class.

VII.

A. The liability of the directors for monetary damages shall be eliminated to the fullest extent under applicable law.

B. To the fullest extent permitted by applicable law, the corporation is authorized to provide indemnification of (and advancement of expenses to) directors, officers and agents of the corporation (and any other persons to which applicable law permits the corporation to provide indemnification) through Bylaw provisions, agreements with such agents or other persons, vote of stockholders or disinterested directors or otherwise in excess of the indemnification and advancement otherwise permitted by such applicable law. If applicable law is amended after approval by the stockholders of this Article VII to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director to the corporation shall be eliminated or limited to the fullest extent permitted by applicable law as so amended.

C. Any repeal or modification of this Article VII shall only be prospective and shall not affect the rights or protections or increase the liability of any officer or director under this Article VII in effect at the time of the alleged occurrence of any act or omission to act giving rise to liability or indemnification. •

VIII.

The corporation reserves the right to amend, alter, change or repeal any provision contained in this Restated Certificate, in the manner now or hereafter prescribed by statute, and all rights conferred upon the stockholders herein are granted subject to this reservation.

IX.

Unless the corporation consents in writing to the selection of an alternative forum, the Court of Chancery in the State of Delaware shall be the sole and exclusive forum for any stockholder (including a beneficial owner) to bring (i) any derivative action or proceeding brought on behalf of the corporation, (ii) any action asserting a claim of breach of fiduciary duty owed by any director, officer or other employee of the corporation to the corporation or the corporation's stockholders, (iii) any action asserting a claim against the corporation, its directors, officers or employees arising pursuant to any provision of the Delaware General Corporation Law or the corporation's certificate of incorporation or bylaws or (iv) any action asserting a claim against the corporation, its directors, officers or employees governed by the internal affairs doctrine, except for, as to each of (i) through (iv) above, any claim as to which the Court of Chancery determines that there is an indispensable party not subject to the jurisdiction of the Court of Chancery (and the indispensable party does not consent to the personal jurisdiction of the Court of Chancery within ten days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery, or for which the Court of Chancery does not have subject matter jurisdiction. If any provision or provisions of this Article IX shall be held to be invalid, illegal or unenforceable as applied to any person or entity or circumstance for any reason whatsoever, then, to the fullest extent permitted by law, the validity, legality and enforceability of such provisions in any other circumstance and of the remaining provisions of this Article IX (including, without limitation, each portion of any sentence of this Article IX containing any such provision held to be invalid, illegal or unenforceable that is not itself held to be invalid, illegal or unenforceable) and the application of such provision to other persons or entities and circumstances shall not in any way be affected or impaired thereby.

*** * * ***

FOUR: This Amended and Restated Certificate of Incorporation has been duly approved by the Board of Directors of the Company.

FIVE: This Amended and Restated Certificate of Incorporation was approved by the holders of the requisite number of shares of said corporation in accordance with Section 228 of the DGCL. This Amended and Restated Certificate of Incorporation has been duly adopted in accordance with the provisions of Sections 242 and 245 of the DGCL by the stockholders of the Company.

[Remainder of this page intentionally left blank]

IN WITNESS WHEREOF, ITERUM THERAPEUTICS US LIMITED has caused this Amended and Restated Certificate of Incorporation to be signed by its President this 17day of November 2015.

ITERUM THERAPEUTICS US LIMITED

/s/ Judith M. Matthews,

Judith M. Matthews, President

BYLAWS

OF

ITERUM THERAPEUTICS US LIMITED

(A DELAWARE CORPORATION)

ARTICLE I

OFFICES

Section 1. **Registered Office**. The registered office of the corporation in the State of Delaware shall be 2711 Centerville Road, Suite 400, City of Wilmington, County of New Castle, 19808 or in such other location as the Board of Directors may from time to time determine or the business of the corporation may require.

Section 2. **Other Offices**. The corporation shall also have and maintain an office or principal place of business at such place as may be fixed by the Board of Directors, and may also have offices at such other places, both within and without the State of Delaware, as the Board of Directors may from time to time determine or the business of the corporation may require.

ARTICLE II

CORPORATE SEAL

Section 3. **Corporate Seal**. The Board of Directors may adopt a corporate seal. Said seal may be used by causing it or a facsimile thereof to be impressed or affixed or reproduced or otherwise.

ARTICLE III

STOCKHOLDERS' MEETINGS

Section 4. **Place of Meetings**. Meetings of the stockholders of the corporation may be held at such place, either within or without the State of Delaware, as may be determined from time to time by the Board of Directors. The Board of Directors may, in its sole discretion, determine that the meeting shall not be held at any place, but may instead be held solely by means of remote communication as provided under the Delaware General Corporation Law ("***DGCL***").

Section 5. **Annual Meeting**.

(a) The annual meeting of the stockholders of the corporation, for the purpose of election of directors and for such other business as may lawfully come before it, shall be held on such date and at such time as may be designated from time to time by the Board of Directors. Nominations of persons for election to the Board of Directors of the corporation and the proposal of business to be considered by the stockholders may be made at an annual meeting of stockholders: (i) pursuant to the corporation's notice of meeting of stockholders; (ii) by or at the direction of the Board of Directors; or (iii) by any stockholder of the corporation who was a stockholder of record at the time of giving of notice provided for in the following paragraph, who is entitled to vote at the meeting and who complied with the notice procedures set forth in this Section.

(b) At an annual meeting of the stockholders, only such business shall be conducted as shall have been properly brought before the meeting. For nominations or other business to be properly brought before an annual meeting by a stockholder pursuant to clause (iii) of paragraph (a) of this Section, (i) the stockholder must have given timely notice thereof in writing to the Secretary of the corporation, (ii) such other business must be a proper matter for stockholder action under the DGCL and applicable law, (iii) if the stockholder, or the beneficial owner on whose behalf any such proposal or nomination is made, has provided the corporation with a Solicitation Notice (as defined in this paragraph), such stockholder or beneficial owner must, in the case of a proposal, have delivered a proxy statement and form of proxy to holders of at least the percentage of the corporation's voting shares required under applicable law to carry any such proposal, or, in the case of a nomination or nominations, have delivered a proxy statement and form of proxy to holders of a percentage of the corporation's voting shares reasonably believed by such stockholder or beneficial owner to be sufficient to elect the nominee or nominees proposed to be nominated by such stockholder, and must, in either case, have included in such materials the Solicitation Notice, and (iv) if no Solicitation Notice relating thereto has been timely provided pursuant to this Section, the stockholder or beneficial owner proposing such business or nomination must not have solicited a number of proxies sufficient to have required the delivery of such a Solicitation Notice under this Section. To be timely, a stockholder's notice shall be delivered to the Secretary at the principal executive offices of the corporation not later than the close of business

on the 90th day nor earlier than the close of business on the 120 th day prior to the first anniversary of the preceding year's annual meeting; *provided, however*, that in the event that the date of the annual meeting is advanced more than 30 days prior to or delayed by more than 30 days after the anniversary of the preceding year's annual meeting, notice by the stockholder to be timely must be so delivered not earlier than the close of business on the 120th day prior to such annual meeting and not later than the close of business on the later of the 90 th day prior to such annual meeting or the 10th day following the day on which public announcement of the date of such meeting is first made. In no event shall the public announcement of an adjournment of an annual meeting commence a new time period for the giving of a stockholder's notice as described above. Such stockholder's notice shall set forth: (A) as to each person whom the stockholder proposed to nominate for election or reelection as a director all information relating to such person that is required to be disclosed in solicitations of proxies for election of directors in an election contest, or is otherwise required, in each case pursuant to Regulation 14A under the Securities Exchange Act of 1934, as amended (the "***1934 Act***"), and Rule 14a-4(d) thereunder (including such person's written consent to being named in the proxy statement as a nominee and to serving as a director if elected); (B) as to any other business that the stockholder proposes to bring before the meeting, a brief description of the business desired to be brought before the meeting, the reasons for conducting such business at the meeting and any material interest in such business of such stockholder and the beneficial owner, if any, on whose behalf the proposal is made; and (C) as to the stockholder giving the notice and the beneficial owner, if any, on whose behalf the nomination or proposal is made (i) the name and address of such stockholder, as they appear on the corporation's books, and of such beneficial owner, (ii) the class and number of shares of the corporation which are owned beneficially and of record by such stockholder and such beneficial owner, and (iii) whether either such stockholder or beneficial owner intends to deliver a proxy statement and form of proxy to holders of, in the case of the proposal, at least the percentage of the corporation's voting shares required under applicable law to carry the proposal or, in the case of a nomination or nominations, a sufficient number of holders of the corporation's voting shares to elect such nominee or nominees (an affirmative statement of such intent, a "***Solicitation Notice***").

(c) Notwithstanding anything in the second sentence of paragraph (b) of this Section to the contrary, in the event that the number of directors to be elected to the Board of Directors of the corporation is increased and there is no public announcement naming all of the nominees for director or specifying the size of the increased Board of Directors made by the corporation at least 100 days prior to the first anniversary of the preceding year's annual meeting, a stockholder's notice required by this Section shall also be considered timely, but only with respect to nominees for any new positions created by such increase, if it shall be delivered to the Secretary at the principal executive offices of the corporation not later than the close of business on the 10th day following the day on which such public announcement is first made by the corporation.

(d) Only such persons who are nominated in accordance with the procedures set forth in this Section (or elected or appointed pursuant to Article IV of these Bylaws) shall be eligible to serve as directors and only such business shall be conducted at a meeting of stockholders as shall have been brought before the meeting in accordance with the procedures set forth in this Section. Except as otherwise provided by law, the Chairman of the meeting shall have the power and duty to determine whether a nomination or any business proposed to be brought before the meeting was made, or proposed, as the case may be, in accordance with the procedures set forth in these Bylaws and, if any proposed nomination or business is not in compliance with these Bylaws, to declare that such defective proposal or nomination shall not be presented for stockholder action at the meeting and shall be disregarded.

(e) Notwithstanding the foregoing provisions of this Section, in order to include information with respect to a stockholder proposal in the proxy statement and form of proxy for a stockholders' meeting, stockholders must provide notice as required by the regulations promulgated under the 1934 Act. Nothing in these Bylaws shall be deemed to affect any rights of stockholders to request inclusion of proposals in the corporation proxy statement pursuant to Rule 14a-8 under the 1934 Act.

(f) For purposes of this Section, "public announcement" shall mean disclosure in a press release reported by the Dow Jones News Service, Associated Press or comparable national news service or in a document publicly filed by the corporation with the Securities and Exchange Commission (the "***SEC***") pursuant to Section 13, 14 or 15(d) of the 1934 Act.

Section 6. Special Meetings.

(a) Special meetings of the stockholders of the corporation may be called, for any purpose or purposes, by (i) the Chairman of the Board of Directors, (ii) the Chief Executive Officer, (iii) the Board of Directors pursuant to a resolution adopted by directors representing a quorum of the Board of Directors or (iv) by the holders of shares entitled to cast not less than 20% of the votes at the meeting, and shall be held at such place, on such date, and at such time as the Board of Directors shall fix.

(b) If a special meeting is properly called by any person or persons other than the Board of Directors, the request shall be in writing, specifying the general nature of the business proposed to be transacted, and shall be delivered personally or sent by certified or registered mail, return receipt requested, or by telegraphic or other facsimile transmission to the Chairman of the Board of Directors, the Chief Executive Officer, or the Secretary of the corporation. No business may be transacted at such special meeting otherwise than specified in such notice. The Board of Directors shall determine the time and place of such special meeting, which shall be held not less than 35 nor more than 120 days after the date of the receipt of the request. Upon determination of the time and place of the meeting, the officer receiving the request shall cause notice to be given to the stockholders entitled to vote, in accordance with the provisions of Section 7 of these Bylaws. Nothing contained in this paragraph (b) shall be construed as limiting, fixing, or affecting the time when a meeting of stockholders called by action of the Board of Directors may be held.

Section 7. Notice of Meetings. Except as otherwise provided by law, notice, given in writing or by electronic transmission, of each meeting of stockholders shall be given not less than 10 nor more than 60 days before the date of the meeting to each stockholder entitled to vote at such meeting, such notice to specify the place, if any, date and hour, in the case of special meetings, the purpose or purposes of the meeting, and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at any such meeting. If mailed, notice is given when deposited in the United States mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the corporation. Notice of the time, place, if any, and purpose of any meeting of stockholders may be waived in writing, signed by the person entitled to notice thereof or by electronic transmission by such person, either before or after such meeting, and will be waived by any stockholder by his or her attendance thereat in person, by remote communication, if applicable, or by proxy, except when the stockholder attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Any stockholder so waiving notice of such meeting shall be bound by the proceedings of any such meeting in all respects as if due notice thereof had been given.

Section 8. Quorum. At all meetings of stockholders, except where otherwise provided by statute or by the Certificate of Incorporation, or by these Bylaws, the presence, in person, by remote communication, if applicable, or by proxy duly authorized, of the holders of a majority of the outstanding shares of stock entitled to vote shall constitute a quorum for the transaction of business. In the absence of a quorum, any meeting of stockholders may be adjourned, from time to time, either by the chairman of the meeting or by vote of the holders of a majority of the shares represented thereat, but no other business shall be transacted at such meeting. The stockholders present at a duly called or convened meeting, at which a quorum is present, may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum. Except as otherwise provided by statute, or by the Certificate of Incorporation or these Bylaws, in all matters other than the election of directors, the affirmative vote of a majority of shares present in person, by remote communication, if applicable, or represented by proxy duly authorized at the meeting and entitled to vote generally on the subject matter shall be the act of the stockholders. Except as otherwise provided by statute, the Certificate of Incorporation or these Bylaws, directors shall be elected by a plurality of the votes of the shares present in person, by remote communication, if applicable, or represented by proxy duly authorized at the meeting and entitled to vote generally on the election of directors. Where a separate vote by a class or classes or series is required, except where otherwise provided by the statute or by the Certificate of Incorporation or these Bylaws, a majority of the outstanding shares of such class or classes or series, present in person, by remote communication, if applicable, or represented by proxy duly authorized, shall constitute a quorum entitled to take action with respect to that vote on that matter. Except where otherwise provided by statute or by the Certificate of Incorporation or these Bylaws, the affirmative vote of the majority (plurality, in the case of the election of directors) of shares of such class or classes or series present in person, by remote communication, if applicable, or represented by proxy at the meeting shall be the act of such class or classes or series.

Section 9. Adjournment and Notice of Adjourned Meetings. Any meeting of stockholders, whether annual or special, may be adjourned from time to time either by the chairman of the meeting or by the vote of a majority of the shares present in person, by remote communication, if applicable, or represented by proxy. When a meeting is adjourned to another time or place, if any, notice need not be given of the adjourned meeting if the time and place, if any, thereof are announced at the meeting at which the adjournment is taken. At the adjourned meeting, the corporation may transact any business which might have been transacted at the original meeting pursuant to the Certificate of Incorporation, these Bylaws or applicable law. If the adjournment is for more than 30 days or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting.

Section 10. Voting Rights. For the purpose of determining those stockholders entitled to vote at any meeting of the stockholders, except as otherwise provided by law, only persons in whose names shares stand on the stock records of the corporation on the record date, as provided in Section 12 of these Bylaws, shall be entitled to vote at any meeting of stockholders. Every person entitled to vote or execute consents shall have the right to do so either in person, by remote communication, if applicable, or by an agent or agents authorized by a proxy granted in accordance with Delaware law. An agent so appointed need not be a stockholder. No proxy shall be voted after three years from its date of creation unless the proxy provides for a longer period.

Section 11. Joint Owners of Stock. If shares or other securities having voting power stand of record in the names of two or more persons, whether fiduciaries, members of a partnership, joint tenants, tenants in common, tenants by the entirety, or otherwise, or if two or more persons have the same fiduciary relationship respecting the same shares, unless the Secretary is given written notice to the contrary and is furnished with a copy of the instrument or order appointing them or creating the relationship wherein it is so provided, their acts with respect to voting (including giving consent pursuant to Section 13) shall have the following effect: (a) if only one votes, his or her act binds all; (b) if more than one votes, the act of the majority so voting binds all; (c) if more than one votes, but the vote is evenly split on any particular matter, each faction may vote the securities in question proportionally, or may apply to the Delaware Court of Chancery for relief as provided in the DGCL, Section 217(b). If the instrument filed with the Secretary shows that any such tenancy is held in unequal interests, a majority or even-split for the purpose of subsection (c) shall be a majority or even-split in interest.

Section 12. List of Stockholders. The Secretary shall prepare and make, at least 10 days before every meeting of stockholders, a complete list of the stockholders entitled to vote at said meeting, arranged in alphabetical order, showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting, on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or during ordinary business hours, at the principal place of business of the corporation. In the event that the corporation determines to make the list available on an electronic network, the corporation may take reasonable steps to ensure that such information is available only to stockholders of the corporation. The list shall be open to examination of any stockholder during the time of the meeting as provided by law.

Section 13. Action Without Meeting.

(a) Unless otherwise provided in the Certificate of Incorporation, any action required by statute to be taken at any annual or special meeting of the stockholders, or any action which may be taken at any annual or special meeting of the stockholders, may be taken without a meeting, without prior notice and without a vote, if a consent in writing, or by electronic transmission setting forth the action so taken, shall be signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote thereon were present and voted.

(b) Every written consent or electronic transmission shall bear the date of signature of each stockholder who signs the consent, and no written consent or electronic transmission shall be effective to take the corporate action referred to therein unless, within 60 days of the earliest dated consent delivered to the corporation in the manner herein required, written consents or electronic transmissions signed by a sufficient number of stockholders to take action are delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are

recorded. Delivery made to a corporation's registered office shall be by hand or by certified or registered mail, return receipt requested.

(c) Prompt notice of the taking of the corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing or by electronic transmission and who, if the action had been taken at a meeting, would have been entitled to notice of the meeting if the record date for such meeting had been the date that written consents signed by a sufficient number of stockholders to take action were delivered to the corporation as provided in Section 228(c) of the DGCL. If the action which is consented to is such as would have required the filing of a certificate under any section of the DGCL if such action had been voted on by stockholders at a meeting thereof, then the certificate filed under such section shall state, in lieu of any statement required by such section concerning any vote of stockholders, that written consent has been given in accordance with Section 228 of the DGCL.

(d) An electronic mail, facsimile or other electronic transmission consenting to an action to be taken and transmitted by a stockholder or proxyholder, shall be deemed to be written, signed and dated for the purposes of this Section, provided that any such electronic mail, facsimile or other electronic transmission sets forth or is delivered with information from which the corporation can determine (i) that the electronic mail, facsimile or other electronic transmission was transmitted by the stockholder or proxyholder or by a person or persons authorized to act for the stockholder and (ii) the date on which such stockholder or proxyholder or authorized person or persons transmitted such electronic mail, facsimile or electronic transmission. The date on which such electronic mail, facsimile or electronic transmission is transmitted shall be deemed to be the date on which such consent was signed. No consent given by electronic mail, facsimile or other electronic transmission shall be deemed to have been delivered until such consent is reproduced in paper form and until such paper form shall be delivered to the corporation by delivery to its registered office in the state of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to a corporation's registered office shall be made by hand or by certified or registered mail, return receipt requested. Notwithstanding the foregoing limitations on delivery, consents given by electronic mail, facsimile or other electronic transmission may be otherwise delivered to the principal place of business of the corporation or to an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded if, to the extent and in the manner provided by resolution of the board of directors of the corporation. Any copy, facsimile or other reliable reproduction of a consent in writing may be substituted or used in lieu of the original writing for any and all purposes for which the original writing could be used, provided that such copy, facsimile or other reproduction shall be a complete reproduction of the entire original writing.

Section 14. Organization.

(a) At every meeting of stockholders, the Chairman of the Board of Directors, or, if a Chairman has not been appointed or is absent, the Chief Executive Officer, or, if the Chief Executive Officer is absent, a chairman of the meeting chosen by a majority in interest of the stockholders entitled to vote, present in person or by proxy, shall act as chairman. The Secretary, or, in his or her absence, an Assistant Secretary directed to do so by the Chief Executive Officer, shall act as secretary of the meeting.

(b) The Board of Directors shall be entitled to make such rules or regulations for the conduct of meetings of stockholders as it shall deem necessary, appropriate or convenient. Subject to such rules and regulations of the Board of Directors, if any, the chairman of the meeting shall have the right and authority to prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are necessary, appropriate or convenient for the proper conduct of the meeting, including, without limitation, establishing an agenda or order of business for the meeting, rules and procedures for maintaining order at the meeting and the safety of those present, limitations on participation in such meeting to stockholders of record of the corporation and their duly authorized and constituted proxies and such other persons as the chairman shall permit, restrictions on entry to the meeting after the time fixed for the commencement thereof, limitations on the time allotted to questions or comments by participants and regulation of the opening and closing of the polls for balloting on matters which are to be voted on by ballot. The date and time of the opening and closing of the polls for each matter upon which the stockholders will vote at the meeting shall be announced at the meeting. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with rules of parliamentary procedure.

ARTICLE IV

DIRECTORS

Section 15. Number and Term of Office.

The authorized number of directors of the corporation shall be fixed by the Board of Directors from time to time.

Directors need not be stockholders unless so required by the Certificate of Incorporation. If for any cause, the directors shall not have been elected at an annual meeting, they may be elected as soon thereafter as convenient.

Section 16. Powers. The business and affairs of the corporation shall be managed by or under the direction of the Board of Directors, except as may be otherwise provided by statute or by the Certificate of Incorporation.

Section 17. Term of Directors. Subject to the rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, directors shall be elected at each annual meeting of stockholders to serve until the next annual meeting of stockholders and his or her successor is duly elected and qualified or until his or her death, resignation or removal. No decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

Section 18. Vacancies. Unless otherwise provided in the Certificate of Incorporation, and subject to the rights of the holders of any series of Preferred Stock, any vacancies on the Board of Directors resulting from death, resignation, disqualification, removal or other causes and any newly created directorships resulting from any increase in the number of directors shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by stockholders, be filled only by the affirmative vote of a majority of the directors then in office, even though less than a quorum of the Board of Directors, or by a sole remaining director; *provided, however*, that whenever the holders of any class or classes of stock or series thereof are entitled to elect one or more directors by the provisions of the Certificate of Incorporation, vacancies and newly created directorships of such class or classes or series shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by stockholders, be filled by a majority of the directors elected by such class or classes or series thereof then in office, or by a sole remaining director so elected. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified. A vacancy in the Board of Directors shall be deemed to exist under this Bylaw in the case of the death, removal or resignation of any director.

Section 19. Resignation. Any director may resign at any time by delivering his or her notice in writing or by electronic transmission to the Secretary, such resignation to specify whether it will be effective at a particular time, upon receipt by the Secretary or at the pleasure of the Board of Directors. If no such specification is made, it shall be deemed effective at the pleasure of the Board of Directors. When one or more directors shall resign from the Board of Directors, effective at a future date, a majority of the directors then in office, including those who have so resigned, shall have power to fill such vacancy or vacancies, the vote thereon to take effect when such resignation or resignations shall become effective, and each Director so chosen shall hold office for the unexpired portion of the term of the Director whose place shall be vacated and until his or her successor shall have been duly elected and qualified.

Section 20. Removal. Subject to any limitations imposed by applicable law, the Board of Directors or any director may be removed from office at any time (i) with cause by the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of capital stock of the corporation entitled to vote generally at an election of directors or (ii) without cause by the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of capital stock of the corporation, entitled to elect such director.

Section 21. Meetings

(a) Regular Meetings. Unless otherwise restricted by the Certificate of Incorporation, regular meetings of the Board of Directors may be held at any time or date and at any place within or without the State of Delaware

which has been designated by the Board of Directors and publicized among all directors, either orally or in writing, including a voice-messaging system or other system designated to record and communicate messages, facsimile, or by electronic mail or other electronic means. No further notice shall be required for a regular meeting of the Board of Directors.

(b) Special Meetings. Unless otherwise restricted by the Certificate of Incorporation, special meetings of the Board of Directors may be held at any time and place within or without the State of Delaware whenever called by the Chairman of the Board, the Chief Executive Officer (if a director), the President (if a director) or any two of the directors.

(c) Meetings by Electronic Communications Equipment. Any member of the Board of Directors, or of any committee thereof, may participate in a meeting by means of conference telephone or other communications equipment by means of which all persons participating in the meeting can hear each other, and participation in a meeting by such means shall constitute presence in person at such meeting.

(d) Notice of Special Meetings. Notice of the time and place of all special meetings of the Board of Directors shall be orally or in writing, by telephone, including a voice messaging system or other system or technology designed to record and communicate messages, facsimile, telegraph or telex, or by electronic mail or other electronic means, during normal business hours, at least 24 hours before the date and time of the meeting. If notice is sent by US mail, it shall be sent by first class mail, postage prepaid at least three days before the date of the meeting. Notice of any meeting may be waived in writing or by electronic transmission at any time before or after the meeting and will be waived by any director by attendance thereat, except when the director attends the meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

(e) Waiver of Notice. The transaction of all business at any meeting of the Board of Directors, or any committee thereof, however called or noticed, or wherever held, shall be as valid as though had at a meeting duly held after regular call and notice, if a quorum be present and if, either before or after the meeting, each of the directors not present who did not receive notice shall sign a written waiver of notice or shall waive notice by electronic transmission. All such waivers shall be filed with the corporate records or made a part of the minutes of the meeting.

Section 22. Quorum and Voting.

(a) Unless the Certificate of Incorporation requires a greater number, a quorum of the Board of Directors shall consist of a majority of the total number of directors then serving; *provided, however*, that such number shall never be less than 1/3 of the total number of directors except that when one director is authorized, then one director shall constitute a quorum. At any meeting, whether a quorum be present or otherwise, a majority of the directors present may adjourn from time to time until the time fixed for the next regular meeting of the Board of Directors, without notice other than by announcement at the meeting. If the Certificate of Incorporation provides that one or more directors shall have more or less than one vote per director on any matter, every reference in this Section to a majority or other proportion of the directors shall refer to a majority or other proportion of the votes of the directors.

(b) At each meeting of the Board of Directors at which a quorum is present, all questions and business shall be determined by the affirmative vote of a majority of the directors present, unless a different vote be required by law, the Certificate of Incorporation or these Bylaws.

Section 23. Action Without Meeting. Unless otherwise restricted by the Certificate of Incorporation or these Bylaws, any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting, if all members of the Board of Directors or committee, as the case may be, consent thereto in writing or by electronic transmission, and such writing or writings or transmission or transmissions are filed with the minutes of proceedings of the Board of Directors or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

Section 24. Fees and Compensation. Directors shall be entitled to such compensation for their services as may be approved by the Board of Directors, including, if so approved, by resolution of the Board of Directors, a fixed sum and expenses of attendance, if any, for attendance at each regular or special meeting of the Board of Directors and at any meeting of a committee of the Board of Directors. Nothing herein contained shall be construed to preclude any director

from serving the corporation in any other capacity as an officer, agent, employee, or otherwise and receiving compensation therefor.

Section 25. Committees.

(a) Executive Committee. The Board of Directors may appoint an Executive Committee to consist of one or more members of the Board of Directors. The Executive Committee, to the extent permitted by law and provided in the resolution of the Board of Directors, shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation, and may authorize the seal of the corporation to be affixed to all papers which may require it; but no such committee shall have the power or authority in reference to (i) approving or adopting, or recommending to the stockholders, any action or matter expressly required by the DGCL to be submitted to stockholders for approval, or (ii) adopting, amending or repealing any bylaw of the corporation.

(b) Other Committees. The Board of Directors may, from time to time, appoint such other committees as may be permitted by law. Such other committees appointed by the Board of Directors shall consist of one or more members of the Board of Directors and shall have such powers and perform such duties as may be prescribed by the resolution or resolutions creating such committees, but in no event shall any such committee have the powers denied to the Executive Committee in these Bylaws.

(c) Term. The Board of Directors, subject to any requirements of any outstanding series of Preferred Stock and the provisions of paragraphs (a) or (b) of this Section may at any time increase or decrease the number of members of a committee or terminate the existence of a committee. The membership of a committee member shall terminate on the date of his or her death or voluntary resignation from the committee or from the Board of Directors. The Board of Directors may at any time for any reason remove any individual committee member and the Board of Directors may fill any committee vacancy created by death, resignation, removal or increase in the number of members of the committee. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee, and, in addition, in the absence or disqualification of any member of a committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not he or they constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of any such absent or disqualified member.

(d) Meetings. Unless the Board of Directors shall otherwise provide, regular meetings of the Executive Committee or any other committee appointed pursuant to this Section shall be held at such times and places as are determined by the Board of Directors, or by any such committee, and when notice thereof has been given to each member of such committee, no further notice of such regular meetings need be given thereafter. Special meetings of any such committee may be held at any place which has been determined from time to time by such committee, and may be called by any director who is a member of such committee, upon notice to the members of such committee of the time and place of such special meeting given in the manner provided for the giving of notice to members of the Board of Directors of the time and place of special meetings of the Board of Directors. Notice of any special meeting of any committee may be waived in writing at any time before or after the meeting and will be waived by any director by attendance thereat, except when the director attends such special meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Unless otherwise provided by the Board of Directors in the resolutions authorizing the creation of the committee, a majority of the authorized number of members of any such committee shall constitute a quorum for the transaction of business, and the act of a majority of those present at any meeting at which a quorum is present shall be the act of such committee.

Section 26. Organization. At every meeting of the directors, the Chairman of the Board of Directors, or, if a Chairman has not been appointed or is absent, the Chief Executive Officer (if a director), or if the Chief Executive Officer is not a director or is absent, the President (if a director), or if the President is not a director or is absent, the most senior Vice President (if a director) or, in the absence of any such person, a chairman of the meeting chosen by a majority of the directors present, shall preside over the meeting. The Secretary, or in his or her absence, any Assistant Secretary directed to do so by the Chief Executive Officer or President, shall act as secretary of the meeting.

ARTICLE V

OFFICERS

Section 27. Officers Designated. The officers of the corporation shall include, if and when designated by the Board of Directors, the Chief Executive Officer, the President, one or more Vice Presidents, the Secretary, the Chief Financial Officer, the Treasurer and the Controller, all of whom shall be elected at the annual organizational meeting of the Board of Directors. The Board of Directors may also appoint one or more Assistant Secretaries, Assistant Treasurers, Assistant Controllers and such other officers and agents with such powers and duties as it shall deem necessary. The Board of Directors may assign such additional titles to one or more of the officers as it shall deem appropriate. Any one person may hold any number of offices of the corporation at any one time unless specifically prohibited therefrom by law. The salaries and other compensation of the officers of the corporation shall be fixed by or in the manner designated by the Board of Directors.

Section 28. Tenure and Duties of Officers.

(a) General. All officers shall hold office at the pleasure of the Board of Directors and until their successors shall have been duly elected and qualified, unless sooner removed. Any officer elected or appointed by the Board of Directors may be removed at any time by the Board of Directors. If the office of any officer becomes vacant for any reason, the vacancy may be filled by the Board of Directors, or by the Chief Executive Officer or other officer if so authorized by the Board of Directors.

(b) Duties of Chairman of the Board of Directors. The Chairman of the Board of Directors, when present, shall preside at all meetings of the stockholders and the Board of Directors. The Chairman of the Board of Directors shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time. If there is no Chief Executive Officer and no President, then the Chairman of the Board of Directors shall also serve as the Chief Executive Officer of the corporation and shall have the powers and duties prescribed in paragraph (c) of this Section.

(c) Duties of Chief Executive Officer. The Chief Executive Officer shall preside at all meetings of the stockholders and (if a director) at all meetings of the Board of Directors, unless the Chairman of the Board of Directors has been appointed and is present. The Chief Executive Officer shall be the chief executive officer of the corporation and shall, subject to the control of the Board of Directors, have general supervision, direction and control of the business and officers of the corporation. The Chief Executive Officer shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time.

(d) Duties of President. In the absence or disability of the Chief Executive Officer or if the office of Chief Executive Officer is vacant, the President shall preside at all meetings of the stockholders and (if a director) at all meetings of the Board of Directors, unless the Chairman of the Board of Directors has been appointed and is present. If the office of Chief Executive Officer is vacant, the President shall be the chief executive officer of the corporation and shall, subject to the control of the Board of Directors, have general supervision, direction and control of the business and officers of the corporation. The President shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time.

(e) Duties of Vice Presidents. The Vice Presidents may assume and perform the duties of the President in the absence or disability of the President or whenever the office of President is vacant. The Vice Presidents shall perform other duties commonly incident to their office and shall also perform such other duties and have such other powers as the Board of Directors or the President shall designate from time to time.

(f) Duties of Secretary. The Secretary shall attend all meetings of the stockholders and of the Board of Directors and shall record all acts and proceedings thereof in the minute book of the corporation. The Secretary shall give notice in conformity with these Bylaws of all meetings of the stockholders and of all meetings of the Board of Directors and any committee thereof requiring notice. The Secretary shall perform all other duties provided for in these Bylaws and other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time. The Chief Executive Officer may direct any Assistant Secretary to

assume and perform the duties of the Secretary in the absence or disability of the Secretary, and each Assistant Secretary shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors or the Chief Executive Officer shall designate from time to time.

(g) Duties of Chief Financial Officer. The Chief Financial Officer shall keep or cause to be kept the books of account of the corporation in a thorough and proper manner and shall render statements of the financial affairs of the corporation in such form and as often as required by the Board of Directors or the Chief Executive Officer. The Chief Financial Officer, subject to the order of the Board of Directors, shall have the custody of all funds and securities of the corporation. The Chief Financial Officer shall perform other duties commonly incident to his or her office and shall also perform such other duties and have such other powers as the Board of Directors or the Chief Executive Officer shall designate from time to time. The Chief Executive Officer may direct the Treasurer or any Assistant Treasurer, or the Controller or any Assistant Controller to assume and perform the duties of the Chief Financial Officer in the absence or disability of the Chief Financial Officer, and each Treasurer and Assistant Treasurer and each Controller and Assistant Controller shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors or the Chief Executive Officer shall designate from time to time.

Section 29. Delegation of Authority. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

Section 30. Resignations. Any officer may resign at any time by giving notice in writing or by electronic transmission notice to the Board of Directors or to the Chief Executive Officer or to the President or to the Secretary. Any such resignation shall be effective when received by the person or persons to whom such notice is given, unless a later time is specified therein, in which event the resignation shall become effective at such later time. Unless otherwise specified in such notice, the acceptance of any such resignation shall not be necessary to make it effective. Any resignation shall be without prejudice to the rights, if any, of the corporation under any contract with the resigning officer.

Section 31. Removal. Any officer may be removed from office at any time, either with or without cause, by the affirmative vote of a majority of the directors in office at the time, or by the unanimous written or electronic consent of the directors in office at the time, or by any committee or superior officers upon whom such power of removal may have been conferred by the Board of Directors.

ARTICLE VI

EXECUTION OF CORPORATE INSTRUMENTS AND VOTING OF SECURITIES OWNED BY THE CORPORATION

Section 32. Execution of Corporate Instruments. The Board of Directors may, in its discretion, determine the method and designate the signatory officer or officers, or other person or persons, to execute on behalf of the corporation any corporate instrument or document, or to sign on behalf of the corporation the corporate name, or to enter into contracts on behalf of the corporation, except where otherwise provided by law or these Bylaws, and such execution or signature shall be binding upon the corporation.

All checks and drafts drawn on banks or other depositaries of funds to the credit of the corporation or on special accounts of the corporation shall be signed by such person or persons as the Board of Directors shall authorize so to do.

Unless authorized or ratified by the Board of Directors or within the agency power of an officer, no officer, agent or employee shall have any power or authority to bind the corporation by any contract or engagement or to pledge its credit or to render it liable for any purpose or for any amount.

Section 33. Voting of Securities Owned by the Corporation. All stock and other securities of other corporations owned or held by the corporation for itself, or for other parties in any capacity, shall be voted, and all proxies with respect thereto shall be executed, by the person authorized so to do by resolution of the Board of Directors, or, in the absence of such authorization, by the Chairman of the Board of Directors, the Chief Executive Officer, the President, or any Vice President.

ARTICLE VII

SHARES OF STOCK

Section 34. Form and Execution of Certificates. The shares of the corporation shall be represented by certificates, or shall be uncertificated. Certificates for the shares of stock, if any, of the corporation shall be in such form as is consistent with the Certificate of Incorporation and applicable law. Every holder of shares of stock in the corporation represented by certificate shall be entitled to have a certificate signed by or in the name of the corporation by the Chairman of the Board of Directors, the Chief Executive Officer, or the President or any Vice President and by the Treasurer or Assistant Treasurer or the Secretary or Assistant Secretary, certifying the number of shares owned by him or her in the corporation. Any or all of the signatures on the certificate may be facsimiles. In case any officer, transfer agent, or registrar who has signed or whose facsimile signature has been placed upon a certificate shall have ceased to be such officer, transfer agent, or registrar before such certificate is issued, it may be issued with the same effect as if he or she were such officer, transfer agent, or registrar at the date of issue.

Section 35. Lost Certificates. A new certificate or certificates shall be issued in place of any certificate or certificates theretofore issued by the corporation alleged to have been lost, stolen, or destroyed, upon the making of an affidavit of that fact by the person claiming the certificate of stock to be lost, stolen, or destroyed. The corporation may require, as a condition precedent to the issuance of a new certificate or certificates, the owner of such lost, stolen, or destroyed certificate or certificates, or the owner's legal representative, to agree to indemnify the corporation in such manner as it shall require or to give the corporation a surety bond in such form and amount as it may direct as indemnity against any claim that may be made against the corporation with respect to the certificate alleged to have been lost, stolen, or destroyed.

Section 36. Restrictions on Transfer.

(a) No holder of any of the shares of stock of the corporation may sell, transfer, assign, pledge, or otherwise dispose of or encumber any of the shares of stock of the corporation or any right or interest therein, whether voluntarily or by operation of law, or by gift or otherwise (each, a "***Transfer***") without the prior written consent of the corporation, upon duly authorized action of its Board of Directors. The corporation may withhold consent for any legitimate corporate purpose, as determined by the Board of Directors. Examples of the basis for the corporation to withhold its consent include, without limitation, (i) if such Transfer to individuals, companies or any other form of entity identified by the corporation as a potential competitor or considered by the corporation to be unfriendly; or (ii) if such Transfer increases the risk of the corporation having a class of security held of record by 2,000 or more persons, or 500 or more persons who are not accredited investors (as such term is defined by the SEC), as described in Section 12(g) of the 1934 Act and any related regulations, or otherwise requiring the corporation to register any class of securities under the 1934 Act; or (iii) if such Transfer would result in the loss of any federal or state securities law exemption relied upon by the corporation in connection with the initial issuance of such shares or the issuance of any other securities; or (iv) if such Transfer is facilitated in any manner by any public posting, message board, trading portal, internet site, or similar method of communication, including without limitation any trading portal or internet site intended to facilitate secondary transfers of securities; or (v) if such Transfer is to be effected in a brokered transaction; or (vi) if such Transfer represents a Transfer of less than all of the shares then held by the stockholder and its affiliates or is to be made to more than a single transferee.

(b) If a stockholder desires to Transfer any shares, then the stockholder shall first give written notice thereof to the corporation. The notice shall name the proposed transferee and state the number of shares to be transferred, the proposed consideration, and all other terms and conditions of the proposed transfer. Any shares proposed to be transferred to which Transfer the corporation has consented pursuant to paragraph (a) of this Section will first be subject to the corporation's right of first refusal located in Section 37 of these Bylaws.

(c) Any Transfer, or purported Transfer, of shares not made in strict compliance with this Section shall be null and void, shall not be recorded on the books of the corporation and shall not be recognized by the corporation.

(d) The foregoing restriction on Transfer shall terminate upon the date securities of the corporation are first offered to the public pursuant to a registration statement filed with, and declared effective by, the SEC under the Securities Act of 1933, as amended (the "***1933 Act***").

(e) The certificates representing shares of stock of the corporation shall bear on their face the following legend so long as the foregoing Transfer restrictions are in effect:

"THE SHARES REPRESENTED BY THIS CERTIFICATE ARE SUBJECT TO A TRANSFER RESTRICTION, AS PROVIDED IN THE BYLAWS OF THE CORPORATION."

Section 37. Right of First Refusal. No stockholder shall Transfer any of the shares of stock of the corporation, except by a Transfer which meets the requirements set forth in this Section 37, in addition to any other restrictions or requirements set forth under applicable law or these Bylaws:

(a) If the stockholder desires to Transfer any of his or her shares of stock, then the stockholder shall first give written notice thereof to the corporation. The notice shall name the proposed transferee and state the number of shares to be transferred, the proposed consideration, and all other terms and conditions of the proposed transfer.

(b) For 30 days following receipt of such notice, the corporation shall have the option to purchase up to all the shares specified in the notice at the price and upon the terms set forth in such notice; *provided, however,* that, with the consent of the stockholder, the corporation shall have the option to purchase a lesser portion of the shares specified in said notice at the price and upon the terms set forth therein. In the event of a gift, property settlement or other Transfer in which the proposed transferee is not paying the full price for the shares, and that is not otherwise exempted from the provisions of this Section, the price shall be deemed to be the fair market value of the stock at such time as determined in good faith by the Board of Directors. In the event the corporation elects to purchase all of the shares or, with consent of the stockholder, a lesser portion of the shares, it shall give written notice to the transferring stockholder of its election and settlement for said shares shall be made as provided below in paragraph (d) of this Section.

(c) The corporation may assign its rights hereunder.

(d) In the event the corporation and/or its assignee(s) elect to acquire any of the shares of the transferring stockholder as specified in said transferring stockholder's notice, the Secretary of the corporation shall so notify the transferring stockholder and settlement thereof shall be made in cash within 30 days after the Secretary of the corporation receives said transferring stockholder's notice; provided that if the terms of payment set forth in said transferring stockholder's notice were other than cash against delivery, the corporation and/or its assignee(s) shall pay for said shares on the same terms and conditions set forth in said transferring stockholder's notice.

(e) In the event the corporation and/or its assignees(s) do not elect to acquire all of the shares specified in the transferring stockholder's notice, said transferring stockholder may, subject to the corporation's approval and all other restrictions on Transfer located in Section 36 of these Bylaws, within the 60-day period following the expiration or waiver of the option rights granted to the corporation and/or its assignees(s) herein, Transfer the shares specified in said transferring stockholder's notice which were not acquired by the corporation and/or its assignees(s) as specified in said transferring stockholder's notice. All shares so sold by said transferring stockholder shall continue to be subject to the provisions of this Bylaw in the same manner as before said Transfer.

(f) Anything to the contrary contained herein notwithstanding, the following transactions shall be exempt from the right of first refusal in paragraph (a) of this Section:

(1) A stockholder's Transfer of any or all shares held either during such stockholder's lifetime or on death by will or intestacy to such stockholder's immediate family or to any custodian or trustee for the account of such stockholder or such stockholder's immediate family or to any limited partnership of which the stockholder, members of such stockholder's immediate family or any trust for the account of such stockholder or such stockholder's immediate family will be the general or limited partner(s) of such partnership. "Immediate family" as used herein shall mean spouse, lineal descendant, father, mother, brother, or sister of the stockholder making such Transfer;

(2) A stockholder's bona fide pledge or mortgage of any shares with a commercial lending institution, provided that any subsequent Transfer of said shares by said institution shall be conducted in the manner set forth in this Bylaw;

(3) A stockholder's Transfer of any or all of such stockholder's shares to the corporation or to any other stockholder of the corporation;

(4) A stockholder's Transfer of any or all of such stockholder's shares to a person who, at the time of such Transfer, is an officer or director of the corporation;

(5) A corporate stockholder's Transfer of any or all of its shares pursuant to and in accordance with the terms of any merger, consolidation, reclassification of shares or capital reorganization of the corporate stockholder, or pursuant to a sale of all or substantially all of the stock or assets of a corporate stockholder;

(6) A corporate stockholder's Transfer of any or all of its shares to any or all of its stockholders; or

(7) A Transfer by a stockholder which is a limited or general partnership to any or all of its partners or former partners in accordance with partnership interests.

In any such case, the transferee, assignee, or other recipient shall receive and hold such stock subject to the provisions of this Section and any other restrictions set forth in these Bylaws, and there shall be no further Transfer of such stock except in accord with this Section and the other provisions of these Bylaws.

(g) The provisions of this Bylaw may be waived with respect to any Transfer either by the corporation, upon duly authorized action of its Board of Directors, or by the stockholders, upon the express written consent of the owners of a majority of the voting power of the corporation (excluding the votes represented by those shares to be transferred by the transferring stockholder). This Bylaw may be amended or repealed either by a duly authorized action of the Board of Directors or by the stockholders, upon the express written consent of the owners of a majority of the voting power of the corporation.

(h) Any Transfer, or purported Transfer, of securities of the corporation shall be null and void unless the terms, conditions, and provisions of this Bylaw are strictly observed and followed.

(i) The foregoing right of first refusal shall terminate upon the date securities of the corporation are first offered to the public pursuant to a registration statement filed with, and declared effective by, the SEC under the Securities Act of 1933, as amended.

(j) The certificates representing shares of stock of the corporation that are subject to the right of first refusal in paragraph (a) of this Section shall bear on their face the following legend so long as the foregoing right of first refusal remains in effect:

> "THE SHARES REPRESENTED BY THIS CERTIFICATE ARE SUBJECT TO A RIGHT OF FIRST REFUSAL OPTION IN FAVOR OF THE CORPORATION AND/OR ITS ASSIGNEE(S), AS PROVIDED IN THE BYLAWS OF THE CORPORATION."

(k) To the extent this Section conflicts with any written agreements between the Company and the stockholder attempting to Transfer shares, such agreement shall control.

Section 38. Fixing Record Dates.

(a) In order that the corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, the Board of Directors may fix, in advance, a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date shall, subject to applicable law, not be more than 60 nor less than 10 days before the date of such meeting. If no record date is fixed by the Board of Directors, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day immediately preceding the day on which notice is given, or if notice is waived, at the close of business on the day immediately preceding the day on which the meeting is held. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to

any adjournment of the meeting; *provided, however,* that the Board of Directors may fix a new record date for the adjourned meeting.

(b) In order that the corporation may determine the stockholders entitled to consent to corporate action in writing without a meeting, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which date shall not be more than 10 days after the date upon which the resolution fixing the record date is adopted by the Board of Directors. Any stockholder of record seeking to have the stockholders authorize or take corporate action by written consent shall, by written notice to the Secretary, request the Board of Directors to fix a record date. The Board of Directors shall promptly, but in all events within 10 days after the date on which such a request is received, adopt a resolution fixing the record date. If no record date has been fixed by the Board of Directors within 10 days of the date on which such a request is received, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting, when no prior action by the Board of Directors is required by applicable law, shall be the first date on which a signed written consent setting forth the action taken or proposed to be taken is delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to the corporation's registered office shall be by hand or by certified or registered mail, return receipt requested. If no record date has been fixed by the Board of Directors and prior action by the Board of Directors is required by law, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting shall be at the close of business on the day on which the Board of Directors adopts the resolution taking such prior action.

(c) In order that the corporation may determine the stockholders entitled to receive payment of any dividend or other distribution or allotment of any rights or the stockholders entitled to exercise any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action, the Board of Directors may fix, in advance, a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted, and which record date shall be not more than 60 days prior to such action. If no record date is fixed, the record date for determining stockholders for any such purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto.

Section 39. Registered Stockholders. The corporation shall be entitled to recognize the exclusive right of a person registered on its books as the owner of shares to receive dividends, and to vote as such owner, and shall not be bound to recognize any equitable or other claim to or interest in such share or shares on the part of any other person whether or not it shall have express or other notice thereof, except as otherwise provided by the laws of Delaware.

ARTICLE VIII

OTHER SECURITIES OF THE CORPORATION

Section 40. Execution of Other Securities. All bonds, debentures and other corporate securities of the corporation, other than stock certificates (covered in Section 34 of these Bylaws), may be signed by the Chairman of the Board of Directors, the Chief Executive Officer, the President or any Vice President, or such other person as may be authorized by the Board of Directors, and the corporate seal impressed thereon or a facsimile of such seal imprinted thereon and attested by the signature of the Secretary or an Assistant Secretary, or the Chief Financial Officer or Treasurer or an Assistant Treasurer; *provided, however,* that where any such bond, debenture or other corporate security shall be authenticated by the manual signature, or where permissible facsimile signature, of a trustee under an indenture pursuant to which such bond, debenture or other corporate security shall be issued, the signatures of the persons signing and attesting the corporate seal on such bond, debenture or other corporate security may be the imprinted facsimile of the signatures of such persons. Interest coupons appertaining to any such bond, debenture or other corporate security, authenticated by a trustee as aforesaid, shall be signed by the Treasurer or an Assistant Treasurer of the corporation or such other person as may be authorized by the Board of Directors, or bear imprinted thereon the facsimile signature of such person. In case any officer who shall have signed or attested any bond, debenture or other corporate security, or whose facsimile signature shall appear thereon or on any such interest coupon, shall have ceased to be such officer before the bond, debenture or other corporate security so signed or attested shall have been delivered, such bond, debenture or other corporate security nevertheless may be adopted by the corporation and issued and delivered as though the person who signed the same or whose facsimile signature shall have been used thereon had not ceased to be such officer of the corporation.

ARTICLE IX

DIVIDENDS

Section 41. Declaration of Dividends. Dividends upon the capital stock of the corporation, subject to the provisions of the Certificate of Incorporation and applicable law, if any, may be declared by the Board of Directors pursuant to law at any regular or special meeting. Dividends may be paid in cash, in property, or in shares of the capital stock, subject to the provisions of the Certificate of Incorporation and applicable law.

Section 42. Dividend Reserve. Before payment of any dividend, there may be set aside out of any funds of the corporation available for dividends such sum or sums as the Board of Directors from time to time, in their absolute discretion, think proper as a reserve or reserves to meet contingencies, or for equalizing dividends, or for repairing or maintaining any property of the corporation, or for such other purpose as the Board of Directors shall think conducive to the interests of the corporation, and the Board of Directors may modify or abolish any such reserve in the manner in which it was created.

ARTICLE X

FISCAL YEAR

Section 43. Fiscal Year. The fiscal year of the corporation shall be fixed by resolution of the Board of Directors.

ARTICLE XI

INDEMNIFICATION

Section 44. Indemnification of Directors, Executive Officers, Other Officers, Employees and Other Agents.

(a) Directors and Executive Officers. The corporation shall indemnify its directors and executive officers (for the purposes of this Article, "executive officers" shall have the meaning defined in Rule 3b-7 promulgated under the 1934 Act) to the fullest extent not prohibited by the DGCL or any other applicable law; *provided, however,* that the corporation may modify the extent of such indemnification by individual contracts with its directors and executive officers; and, *provided, further,* that the corporation shall not be required to indemnify any director or executive officer in connection with any proceeding (or part thereof) initiated by such person unless (i) such indemnification is expressly required to be made by law, (ii) the proceeding was authorized by the Board of Directors of the corporation, (iii) such indemnification is provided by the corporation, in its sole discretion, pursuant to the powers vested in the corporation under the DGCL or any other applicable law or (iv) such indemnification is required to be made under paragraph (d) of this Section.

(b) Other Officers, Employees and Other Agents. The corporation shall have power to indemnify its other officers, employees and other agents as set forth in the DGCL or any other applicable law. The Board of Directors shall have the power to delegate the determination of whether indemnification shall be given to any such person except executive officers to such officers or other persons as the Board of Directors shall determine.

(c) Expenses. The corporation shall advance to any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that such person is or was a director or executive officer of the corporation, or is or was serving at the request of the corporation as a director or executive officer of another corporation, partnership, joint venture, trust or other enterprise, prior to the final disposition of the proceeding, promptly following request therefor, all expenses incurred by any director or executive officer in connection with such proceeding, *provided, however*, that, if the DGCL requires, an advancement of expenses incurred by a director or officer in his or her capacity as a director or officer (and not in any other capacity in which service was or is rendered by such indemnitee, including, without limitation, service to an employee benefit plan) shall be made only upon delivery to the corporation of an undertaking, by or on behalf of such

indemnitee, to repay all amounts so advanced if it shall ultimately be determined by final judicial decision from which there is no further right to appeal that such indemnitee is not entitled to be indemnified for such expenses under this Section or otherwise.

Notwithstanding the foregoing, unless otherwise determined pursuant to paragraph (e) of this Section, no advance shall be made by the corporation to an executive officer of the corporation (except by reason of the fact that such executive officer is or was a director of the corporation, in which event this paragraph shall not apply) in any action, suit or proceeding, whether civil, criminal, administrative or investigative, if a determination is reasonably and promptly made (i) by a majority vote of a quorum consisting of directors who were not parties to the proceeding, even if not a quorum, or (ii) by a committee of such directors designated by a majority of such directors, even though less than a quorum, or (iii) if there are no such directors, or such directors so direct, by independent legal counsel in a written opinion, that the facts known to the decision-making party at the time such determination is made demonstrate clearly and convincingly that such person acted in bad faith or in a manner that such person did not believe to be in or not opposed to the best interests of the corporation.

(d) Enforcement. Without the necessity of entering into an express contract, all rights to indemnification and advances to directors and executive officers under this Section shall be deemed to be contractual rights and be effective to the same extent and as if provided for in a contract between the corporation and the director or executive officer. Any right to indemnification or advances granted by this Section to a director or executive officer shall be enforceable by or on behalf of the person holding such right in any court of competent jurisdiction if (i) the claim for indemnification or advances is denied, in whole or in part, or (ii) no disposition of such claim is made within 90 days of request therefor. The claimant in such enforcement action, if successful in whole or in part, shall be entitled to be paid also the expense of prosecuting the claim. In connection with any claim for indemnification, the corporation shall be entitled to raise as a defense to any such action that the claimant has not met the standards of conduct that make it permissible under the DGCL or any other applicable law for the corporation to indemnify the claimant for the amount claimed. In connection with any claim by an executive officer of the corporation (except in any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that such executive officer is or was a director of the corporation) for advances, the corporation shall be entitled to raise as a defense as to any such action clear and convincing evidence that such person acted in bad faith or in a manner that such person did not believe to be in or not opposed to the best interests of the corporation, or with respect to any criminal action or proceeding that such person acted without reasonable cause to believe that his or her conduct was lawful. Neither the failure of the corporation (including its Board of Directors, independent legal counsel or its stockholders) to have made a determination prior to the commencement of such action that indemnification of the claimant is proper in the circumstances because he has met the applicable standard of conduct set forth in the DGCL or any other applicable law, nor an actual determination by the corporation (including its Board of Directors, independent legal counsel or its stockholders) that the claimant has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that claimant has not met the applicable standard of conduct.

(e) Non-Exclusivity of Rights. The rights conferred on any person by this Section shall not be exclusive of any other right which such person may have or hereafter acquire under any applicable statute, provision of the Certificate of Incorporation, Bylaws, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his or her official capacity and as to action in another capacity while holding office. The corporation is specifically authorized to enter into individual contracts with any or all of its directors, officers, employees or agents respecting indemnification and advances, to the fullest extent not prohibited by the DGCL or any other applicable law.

(f) Survival of Rights. The rights conferred on any person by this Section shall continue as to a person who has ceased to be a director or executive officer and shall inure to the benefit of the heirs, executors and administrators of such a person.

(g) Insurance. To the fullest extent permitted by the DGCL, or any other applicable law, the corporation, upon approval by the Board of Directors, may purchase insurance on behalf of any person required or permitted to be indemnified pursuant to this Section.

(h) Amendments. Any repeal or modification of this Section shall only be prospective and shall not affect the rights under this Bylaw in effect at the time of the alleged occurrence of any action or omission to act that is the cause of any proceeding against any agent of the corporation.

(i) **Saving Clause**. If this Section or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the corporation shall nevertheless indemnify each director and executive officer to the full extent not prohibited by any applicable portion of this Bylaw that shall not have been invalidated, or by any other applicable law. If this Section shall be invalid due to the application of the indemnification provisions of another jurisdiction, then the corporation shall indemnify each director and executive officer to the full extent under applicable law.

(j) **Certain Definitions**. For the purposes of this Section, the following definitions shall apply:

(1) The term "proceeding" shall be broadly construed and shall include, without limitation, the investigation, preparation, prosecution, defense, settlement, arbitration and appeal of, and the giving of testimony in, any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative.

(2) The term "expenses" shall be broadly construed and shall include, without limitation, court costs, attorneys' fees, witness fees, fines, amounts paid in settlement or judgment and any other costs and expenses of any nature or kind incurred in connection with any proceeding.

(3) The term the "corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under the provisions of this Section with respect to the resulting or surviving corporation as he would have with respect to such constituent corporation if its separate existence had continued.

(4) References to a "director," "executive officer," "officer," "employee," or "agent" of the corporation shall include, without limitation, situations where such person is serving at the request of the corporation as, respectively, a director, executive officer, officer, employee, trustee or agent of another corporation, partnership, joint venture, trust or other enterprise.

(5) References to "other enterprises" shall include employee benefit plans; references to "fines" shall include any excise taxes assessed on a person with respect to an employee benefit plan; and references to "serving at the request of the corporation" shall include any service as a director, officer, employee or agent of the corporation which imposes duties on, or involves services by, such director, officer, employee, or agent with respect to an employee benefit plan, its participants, or beneficiaries; and a person who acted in good faith and in a manner he reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner "not opposed to the best interests of the corporation" as referred to in this Section.

ARTICLE XII

NOTICES

Section 45. **Notices**.

(a) **Notice to Stockholders**. Written notice to stockholders of stockholder meetings shall be given as provided in Section 7 of these Bylaws. Without limiting the manner by which notice may otherwise be given effectively to stockholders under any agreement or contract with such stockholder, and except as otherwise required by law, written notice to stockholders for purposes other than stockholder meetings may be sent by United States mail or nationally recognized overnight courier, or by facsimile, telegraph or telex or by electronic mail or other electronic means.

(b) **Notice to Directors**. Any notice required to be given to any director may be given by the method stated in paragraph (a) of this Section, or as provided for in Section 21 of these Bylaws. If such notice is not delivered personally, it shall be sent to such address as such director shall have filed in writing with the Secretary, or, in the absence of such filing, to the last known post office address of such director.

(c) **Affidavit of Mailing**. An affidavit of mailing, executed by a duly authorized and competent employee of the corporation or its transfer agent appointed with respect to the class of stock affected or other agent, specifying the name and address or the names and addresses of the stockholder or stockholders, or director or directors, to whom any such notice or notices was or were given, and the time and method of giving the same, shall in the absence of fraud, be prima facie evidence of the facts therein contained.

(d) **Methods of Notice**. It shall not be necessary that the same method of giving notice be employed in respect of all recipients of notice, but one permissible method may be employed in respect of any one or more, and any other permissible method or methods may be employed in respect of any other or others.

(e) **Notice to Person with Whom Communication Is Unlawful**. Whenever notice is required to be given, under any provision of law or of the Certificate of Incorporation or Bylaws of the corporation, to any person with whom communication is unlawful, the giving of such notice to such person shall not be required and there shall be no duty to apply to any governmental authority or agency for a license or permit to give such notice to such person. Any action or meeting which shall be taken or held without notice to any such person with whom communication is unlawful shall have the same force and effect as if such notice had been duly given. In the event that the action taken by the corporation is such as to require the filing of a certificate under any provision of the DGCL, the certificate shall state, if such is the fact and if notice is required, that notice was given to all persons entitled to receive notice except such persons with whom communication is unlawful.

(f) **Notice to Stockholders Sharing an Address**. Except as otherwise prohibited under DGCL, any notice given under the provisions of DGCL, the Certificate of Incorporation or the Bylaws shall be effective if given by a single written notice to stockholders who share an address if consented to by the stockholders at that address to whom such notice is given. Such consent shall have been deemed to have been given if such stockholder fails to object in writing to the corporation within 60 days of having been given notice by the corporation of its intention to send the single notice. Any consent shall be revocable by the stockholder by written notice to the corporation.

ARTICLE XIII

AMENDMENTS

Section 46. **Amendments**. The Board of Directors is expressly empowered to adopt, amend or repeal Bylaws of the corporation. The stockholders shall also have power to adopt, amend or repeal the Bylaws of the corporation; *provided, however*, that, in addition to any vote of the holders of any class or series of stock of the corporation required by law or by the Certificate of Incorporation, such action by stockholders shall require the affirmative vote of the holders of at least a majority of the voting power of all of the then-outstanding shares of the capital stock of the corporation entitled to vote generally in the election of directors, voting together as a single class.

ARTICLE XIV

LOANS TO OFFICERS

Section 47. **Loans to Officers**. Except as otherwise prohibited under applicable law, the corporation may lend money to, or guarantee any obligation of, or otherwise assist any officer or other employee of the corporation or of its subsidiaries, including any officer or employee who is a Director of the corporation or its subsidiaries, whenever, in the judgment of the Board of Directors, such loan, guarantee or assistance may reasonably be expected to benefit the corporation. The loan, guarantee or other assistance may be with or without interest and may be unsecured, or secured in such manner as the Board of Directors shall approve, including, without limitation, a pledge of shares of stock of the corporation. Nothing in these Bylaws shall be deemed to deny, limit or restrict the powers of guaranty or warranty of the corporation at common law or under any statute.

ARTICLE XV

MISCELLANEOUS

Section 48. **Forum**. Unless the corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of the corporation; (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the corporation to the corporation or the corporation's stockholders; (iii) any action asserting a claim against the corporation or any director or officer or other employee of the corporation arising pursuant to any provision of the DGCL, the certificate of incorporation or the Bylaws of the corporation; or (iv) any action asserting a claim against the corporation or any director or officer or other employee of the corporation governed by the internal affairs doctrine.

Exhibit 3.7

CERTIFICATE OF AMENDMENT OF

CERTIFICATE OF INCORPORATION OF

ITERUM THERAPEUTICS US HOLDINGS LIMITED

ITERUM THERAPEUTICS US HOLDINGS LIMITED, a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the ***"Corporation"),*** hereby certifies that:

FIRST: The name of the Corporation is Iterum Therapeutics US Holdings Limited.

SECOND: The date on which the Certificate of Incorporation of the Corporation was originally filed with the Secretary of State of the State of Delaware is January 29, 2018.

THIRD: The Corporation has not received any payment for any of its stock.

FOURTH: The Sole Incorporator of the Corporation, acting in accordance with the provisions of Sections 107 and 241 of the General Corporation Law of the State of Delaware, adopted resolutions amending its Certificate of Incorporation as follows:

Article I shall be amended and restated to read in its entirety as follows:

"The name of this corporation is Iterum Therapeutics US Holding Limited (the ***"Company"*** or the ***"Corporation")"***

IN WITNESS WHEREOF, This Certificate of Amendment has been subscribed as of this 5th day of February, 2018 by the undersigned who affirms that the statements made herein are true and correct.

ITERUM THERAPEUTICS US HOLDINGS LIMITED

/s/ Colleen Burns

COLLEEN BURNS
Sole Incorporator

BYLAWS
OF
ITERUM THERAPEUTICS US HOLDING LIMITED (A DELAWARE CORPORATION)

ARTICLE I

OFFICES

Section 1. **Registered Office**. The registered office of the corporation in the State of Delaware shall be 251 Little Falls Drive, City of Wilmington, County of New Castle, 19808 or in such other location as the Board of Directors may from time to time determine or the business of the corporation may require.

Section 2. **Other Offices**. The corporation shall also have and maintain an office or principal place of business at such place as may be fixed by the Board of Directors, and may also have offices at such other places, both within and without the State of Delaware, as the Board of Directors may from time to time determine or the business of the corporation may require.

ARTICLE II

CORPORATE SEAL

Section 3. **Corporate Seal**. The Board of Directors may adopt a corporate seal. Said seal may be used by causing it or a facsimile thereof to be impressed or affixed or reproduced or otherwise.

ARTICLE III

STOCKHOLDERS' MEETINGS

Section 4. **Place of Meetings**. Meetings of the stockholders of the corporation may be held at such place, either within or without the State of Delaware, as may be determined from time to time by the Board of Directors. The Board of Directors may, in its sole discretion, determine that the meeting shall not be held at any place, but may instead be held solely by means of remote communication as provided under the Delaware General Corporation Law ("***DGCL***").

Section 5. **Annual Meeting**.

(a) The annual meeting of the stockholders of the corporation, for the purpose of election of directors and for such other business as may lawfully come before it, shall be held on such date and at such time as may be designated from time to time by the Board of Directors. Nominations of persons for election to the Board of Directors of the corporation and the proposal of business to be considered by the stockholders may be made at an annual meeting of stockholders: (i) pursuant to the corporation's notice of meeting of stockholders; (ii) by or at the direction of the Board of Directors; or (iii) by any stockholder of the corporation who was a stockholder of record at the time of giving of notice provided for in the following paragraph, who is entitled to vote at the meeting and who complied with the notice procedures set forth in this Section.

(b) At an annual meeting of the stockholders, only such business shall be conducted as shall have been properly brought before the meeting. For nominations or other business to be properly brought before an annual meeting by a stockholder pursuant to clause (iii) of paragraph (a) of this Section, (i) the stockholder must have given timely notice thereof in writing to the Secretary of the corporation, (ii) such other business must be a proper matter for stockholder action under the DGCL and applicable law, (iii) if the stockholder, or the beneficial owner on whose behalf any such proposal or nomination is made, has provided the corporation with a Solicitation Notice (as defined in this paragraph), such stockholder or beneficial owner must, in the case of a proposal, have delivered a proxy statement and form of proxy to holders of at least the percentage of the corporation's voting shares required under applicable law to carry any such proposal, or, in the case of a nomination or nominations, have delivered a proxy statement and form of proxy to holders of a percentage of the corporation's voting shares reasonably believed by such stockholder or beneficial owner to be sufficient to elect the nominee or nominees proposed to be nominated by such stockholder, and must, in either case, have included in such materials the Solicitation Notice, and (iv) if no Solicitation Notice relating thereto has been timely provided pursuant to this Section, the stockholder or beneficial owner proposing such business or nomination must not have solicited a number of proxies sufficient to have required the delivery of such a Solicitation Notice under this Section. To be timely, a stockholder's notice shall be delivered to the Secretary at the principal executive offices of the corporation not later than

the close of business on the 90th day nor earlier than the close of business on the 120th day prior to the first anniversary of the preceding year's annual meeting; *provided, however*, that in the event that the date of the annual meeting is advanced more than 30 days prior to or delayed by more than 30 days after the anniversary of the preceding year's annual meeting, notice by the stockholder to be timely must be so delivered not earlier than the close of business on the 120th day prior to such annual meeting and not later than the close of business on the later of the 90th day prior to such annual meeting or the 10th day following the day on which public announcement of the date of such meeting is first made. In no event shall the public announcement of an adjournment of an annual meeting commence a new time period for the giving of a stockholder's notice as described above. Such stockholder's notice shall set forth: (A) as to each person whom the stockholder proposed to nominate for election or reelection as a director all information relating to such person that is required to be disclosed in solicitations of proxies for election of directors in an election contest, or is otherwise required, in each case pursuant to Regulation 14A under the Securities Exchange Act of 1934, as amended (the "***1934 Act***"), and Rule 14a-4(d) thereunder (including such person's written consent to being named in the proxy statement as a nominee and to serving as a director if elected); (B) as to any other business that the stockholder proposes to bring before the meeting, a brief description of the business desired to be brought before the meeting, the reasons for conducting such business at the meeting and any material interest in such business of such stockholder and the beneficial owner, if any, on whose behalf the proposal is made; and (C) as to the stockholder giving the notice and the beneficial owner, if any, on whose behalf the nomination or proposal is made (i) the name and address of such stockholder, as they appear on the corporation's books, and of such beneficial owner, (ii) the class and number of shares of the corporation which are owned beneficially and of record by such stockholder and such beneficial owner, and (iii) whether either such stockholder or beneficial owner intends to deliver a proxy statement and form of proxy to holders of, in the case of the proposal, at least the percentage of the corporation's voting shares required under applicable law to carry the proposal or, in the case of a nomination or nominations, a sufficient number of holders of the corporation's voting shares to elect such nominee or nominees (an affirmative statement of such intent, a "***Solicitation Notice***").

(c) Notwithstanding anything in the second sentence of paragraph (b) of this Section to the contrary, in the event that the number of directors to be elected to the Board of Directors of the corporation is increased and there is no public announcement naming all of the nominees for director or specifying the size of the increased Board of Directors made by the corporation at least 100 days prior to the first anniversary of the preceding year's annual meeting, a stockholder's notice required by this Section shall also be considered timely, but only with respect to nominees for any new positions created by such increase, if it shall be delivered to the Secretary at the principal executive offices of the corporation not later than the close of business on the 10th day following the day on which such public announcement is first made by the corporation.

(d) Only such persons who are nominated in accordance with the procedures set forth in this Section (or elected or appointed pursuant to Article IV of these Bylaws) shall be eligible to serve as directors and only such business shall be conducted at a meeting of stockholders as shall have been brought before the meeting in accordance with the procedures set forth in this Section. Except as otherwise provided by law, the Chairman of the meeting shall have the power and duty to determine whether a nomination or any business proposed to be brought before the meeting was made, or proposed, as the case may be, in accordance with the procedures set forth in these Bylaws and, if any proposed nomination or business is not in compliance with these Bylaws, to declare that such defective proposal or nomination shall not be presented for stockholder action at the meeting and shall be disregarded.

(e) Notwithstanding the foregoing provisions of this Section, in order to include information with respect to a stockholder proposal in the proxy statement and form of proxy for a stockholders' meeting, stockholders must provide notice as required by the regulations promulgated under the 1934 Act. Nothing in these Bylaws shall be deemed to affect any rights of stockholders to request inclusion of proposals in the corporation proxy statement pursuant to Rule 14a-8 under the 1934 Act.

(f) For purposes of this Section, "public announcement" shall mean disclosure in a press release reported by the Dow Jones News Service, Associated Press or comparable national news service or in a document publicly filed by the corporation with the Securities and Exchange Commission (the "***SEC***") pursuant to Section 13, 14 or 15(d) of the 1934 Act.

Section 6. Special Meetings.

(a) Special meetings of the stockholders of the corporation may be called, for any purpose or purposes, by (i) the Chairman of the Board of Directors, (ii) the Chief Executive Officer, (iii) the Board of Directors pursuant to a resolution adopted by directors representing a quorum of the Board of Directors or (iv) by the holders of shares entitled to cast not less than 20% of the votes at the meeting, and shall be held at such place, on such date, and at such time as the Board of Directors shall fix.

(b) If a special meeting is properly called by any person or persons other than the Board of Directors, the request shall be in writing, specifying the general nature of the business proposed to be transacted, and shall be delivered personally or sent by certified or registered mail, return receipt requested, or by telegraphic or other facsimile transmission to the Chairman of the Board of Directors, the Chief Executive Officer, or the Secretary of the corporation. No business may be transacted at such special meeting otherwise than specified in such notice. The Board of Directors shall determine the time and place of such special meeting, which shall be held not less than 35 nor more than 120 days after the date of the receipt of the request. Upon determination of the time and place of the meeting, the officer receiving the request shall cause notice to be given to the stockholders entitled to vote, in accordance with the provisions of Section 7 of these Bylaws. Nothing contained in this paragraph (b) shall be construed as limiting, fixing, or affecting the time when a meeting of stockholders called by action of the Board of Directors may be held.

Section 7. Notice of Meetings. Except as otherwise provided by law, notice, given in writing or by electronic transmission, of each meeting of stockholders shall be given not less than 10 nor more than 60 days before the date of the meeting to each stockholder entitled to vote at such meeting, such notice to specify the place, if any, date and hour, in the case of special meetings, the purpose or purposes of the meeting, and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at any such meeting. If mailed, notice is given when deposited in the United States mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the corporation. Notice of the time, place, if any, and purpose of any meeting of stockholders may be waived in writing, signed by the person entitled to notice thereof or by electronic transmission by such person, either before or after such meeting, and will be waived by any stockholder by his or her attendance thereat in person, by remote communication, if applicable, or by proxy, except when the stockholder attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Any stockholder so waiving notice of such meeting shall be bound by the proceedings of any such meeting in all respects as if due notice thereof had been given.

Section 8. Quorum. At all meetings of stockholders, except where otherwise provided by statute or by the Certificate of Incorporation, or by these Bylaws, the presence, in person, by remote communication, if applicable, or by proxy duly authorized, of the holders of a majority of the outstanding shares of stock entitled to vote shall constitute a quorum for the transaction of business. In the absence of a quorum, any meeting of stockholders may be adjourned, from time to time, either by the chairman of the meeting or by vote of the holders of a majority of the shares represented thereat, but no other business shall be transacted at such meeting. The stockholders present at a duly called or convened meeting, at which a quorum is present, may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum. Except as otherwise provided by statute, or by the Certificate of Incorporation or these Bylaws, in all matters other than the election of directors, the affirmative vote of a majority of shares present in person, by remote communication, if applicable, or represented by proxy duly authorized at the meeting and entitled to vote generally on the subject matter shall be the act of the stockholders. Except as otherwise provided by statute, the Certificate of Incorporation or these Bylaws, directors shall be elected by a plurality of the votes of the shares present in person, by remote communication, if applicable, or represented by proxy duly authorized at the meeting and entitled to vote generally on the election of directors. Where a separate vote by a class or classes or series is required, except where otherwise provided by the statute or by the Certificate of Incorporation or these Bylaws, a majority of the outstanding shares of such class or classes or series, present in person, by remote communication, if applicable, or represented by proxy duly authorized, shall constitute a quorum entitled to take action with respect to that vote on that matter. Except where otherwise provided by statute or by the Certificate of Incorporation or these Bylaws, the affirmative vote of the majority (plurality, in the case of the election of directors) of shares of such class or classes or series present in person, by remote communication, if applicable, or represented by proxy at the meeting shall be the act of such class or classes or series.

Section 9. Adjournment and Notice of Adjourned Meetings. Any meeting of stockholders, whether annual or special, may be adjourned from time to time either by the chairman of the meeting or by the vote of a majority of the shares present in person, by remote communication, if applicable, or represented by proxy. When a meeting is adjourned to another time or place, if any, notice need not be given of the adjourned meeting if the time and place, if any, thereof are announced at the meeting at which the adjournment is taken. At the adjourned meeting, the corporation may transact any business which might have been transacted at the original meeting pursuant to the Certificate of Incorporation, these Bylaws or applicable law. If the adjournment is for more than 30 days or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting.

Section 10. Voting Rights. For the purpose of determining those stockholders entitled to vote at any meeting of the stockholders, except as otherwise provided by law, only persons in whose names shares stand on the stock records of the corporation on the record date, as provided in Section 12 of these Bylaws, shall be entitled to vote at any meeting of stockholders. Every person entitled to vote or execute consents shall have the right to do so either in person, by remote communication, if applicable, or by an agent or agents authorized by a proxy granted in accordance with Delaware law. An agent so appointed need not be a stockholder. No proxy shall be voted after three years from its date of creation unless the proxy provides for a longer period.

Section 11. Joint Owners of Stock. If shares or other securities having voting power stand of record in the names of two or more persons, whether fiduciaries, members of a partnership, joint tenants, tenants in common, tenants by the entirety, or otherwise, or if two or more persons have the same

fiduciary relationship respecting the same shares, unless the Secretary is given written notice to the contrary and is furnished with a copy of the instrument or order appointing them or creating the relationship wherein it is so provided, their acts with respect to voting (including giving consent pursuant to Section 13) shall have the following effect: (a) if only one votes, his or her act binds all; (b) if more than one votes, the act of the majority so voting binds all; (c) if more than one votes, but the vote is evenly split on any particular matter, each faction may vote the securities in question proportionally, or may apply to the Delaware Court of Chancery for relief as provided in the DGCL, Section 217(b). If the instrument filed with the Secretary shows that any such tenancy is held in unequal interests, a majority or even-split for the purpose of subsection (c) shall be a majority or even-split in interest.

Section 12. List of Stockholders. The Secretary shall prepare and make, at least 10 days before every meeting of stockholders, a complete list of the stockholders entitled to vote at said meeting, arranged in alphabetical order, showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting, on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or during ordinary business hours, at the principal place of business of the corporation. In the event that the corporation determines to make the list available on an electronic network, the corporation may take reasonable steps to ensure that such information is available only to stockholders of the corporation. The list shall be open to examination of any stockholder during the time of the meeting as provided by law.

Section 13. Action Without Meeting.

(a) Unless otherwise provided in the Certificate of Incorporation, any action required by statute to be taken at any annual or special meeting of the stockholders, or any action which may be taken at any annual or special meeting of the stockholders, may be taken without a meeting, without prior notice and without a vote, if a consent in writing, or by electronic transmission setting forth the action so taken, shall be signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote thereon were present and voted.

(b) Every written consent or electronic transmission shall bear the date of signature of each stockholder who signs the consent, and no written consent or electronic transmission shall be effective to take the corporate action referred to therein unless, within 60 days of the earliest dated consent delivered to the corporation in the manner herein required, written consents or electronic transmissions signed by a sufficient number of stockholders to take action are delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or

an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to a corporation's registered office shall be by hand or by certified or registered mail, return receipt requested.

(c) Prompt notice of the taking of the corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing or by electronic transmission and who, if the action had been taken at a meeting, would have been entitled to notice of the meeting if the record date for such meeting had been the date that written consents signed by a sufficient number of stockholders to take action were delivered to the corporation as provided in Section 228(c) of the DGCL. If the action which is consented to is such as would have required the filing of a certificate under any section of the DGCL if such action had been voted on by stockholders at a meeting thereof, then the certificate filed under such section shall state, in lieu of any statement required by such section concerning any vote of stockholders, that written consent has been given in accordance with Section 228 of the DGCL.

(d) An electronic mail, facsimile or other electronic transmission consenting to an action to be taken and transmitted by a stockholder or proxyholder, shall be deemed to be written, signed and dated for the purposes of this Section, provided that any such electronic mail, facsimile or other electronic transmission sets forth or is delivered with information from which the corporation can determine (i) that the electronic mail, facsimile or other electronic transmission was transmitted by the stockholder or proxyholder or by a person or persons authorized to act for the stockholder and (ii) the date on which such stockholder or proxyholder or authorized person or persons transmitted such electronic mail, facsimile or electronic transmission. The date on which such electronic mail, facsimile or electronic transmission is transmitted shall be deemed to be the date on which such consent was signed. No consent given by electronic mail, facsimile or other electronic transmission shall be deemed to have been delivered until such consent is reproduced in paper form and until such paper form shall be delivered to the corporation by delivery to its registered office in the state of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to a corporation's registered office shall be made by hand or by certified or registered mail, return receipt requested. Notwithstanding the foregoing limitations on delivery, consents given by electronic mail, facsimile or other electronic transmission may be otherwise delivered to the principal place of business of the corporation or to an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded if, to the extent and in the manner provided by resolution of the board of directors of the corporation. Any copy, facsimile or other reliable reproduction of a consent in writing may be substituted or used in lieu of the original writing for any and all purposes for which the original writing could be used, provided that such copy, facsimile or other reproduction shall be a complete reproduction of the entire original writing.

Section 14. Organization.

(a) At every meeting of stockholders, the Chairman of the Board of Directors, or, if a Chairman has not been appointed or is absent, the Chief Executive Officer, or, if the Chief Executive Officer is absent, a chairman of the meeting chosen by a majority in interest of the stockholders entitled to vote, present in person or by proxy, shall act as chairman. The Secretary, or, in his or her absence, an Assistant Secretary directed to do so by the Chief Executive Officer, shall act as secretary of the meeting.

(b) The Board of Directors shall be entitled to make such rules or regulations for the conduct of meetings of stockholders as it shall deem necessary, appropriate or convenient. Subject to such rules and regulations of the Board of Directors, if any, the chairman of the meeting shall have the right and authority to prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are necessary, appropriate or convenient for the proper conduct of the meeting, including, without limitation, establishing an agenda or order of business for the meeting, rules and procedures for maintaining order at the meeting and the safety of those present, limitations on participation in such meeting to stockholders of record of the corporation and their duly authorized and constituted proxies and such other persons as the chairman shall permit, restrictions on entry to the meeting after the time fixed for the commencement thereof, limitations on the time allotted to questions or comments by participants and regulation of the opening and closing of the polls for balloting on matters which are to be voted on by ballot. The date and time of the opening and closing of the polls for each matter upon which the stockholders will vote at the meeting shall be announced at the meeting. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with rules of parliamentary procedure.

ARTICLE IV

DIRECTORS

Section 15. Number and Term of Office.

The authorized number of directors of the corporation shall be fixed by the Board of Directors from time to time.

Directors need not be stockholders unless so required by the Certificate of Incorporation. If for any cause, the directors shall not have been elected at an annual meeting, they may be elected as soon thereafter as convenient.

Section 16. Powers. The business and affairs of the corporation shall be managed by or under the direction of the Board of Directors, except as may be otherwise provided by statute or by the Certificate of Incorporation.

Section 17. Term of Directors. Subject to the rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, directors shall be elected at each annual meeting of stockholders to serve until the next annual meeting of stockholders and his or her successor is duly elected and qualified or until his or her death, resignation or removal. No decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

Section 18. Vacancies. Unless otherwise provided in the Certificate of Incorporation, and subject to the rights of the holders of any series of Preferred Stock, any vacancies on the Board of Directors resulting from death, resignation, disqualification, removal or other causes and any newly created directorships resulting from any increase in the number of directors shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by stockholders, be filled only by the affirmative vote of a majority of the directors then in office, even though less than a quorum of the Board of Directors, or by a sole remaining director; *provided, however*, that whenever the holders of any class or classes of stock or series thereof are entitled to elect one or more directors by the provisions of the Certificate of Incorporation, vacancies and newly created directorships of such class or classes or series shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by stockholders, be filled by a majority of the directors elected by such class or classes or series thereof then in office, or by a sole remaining director so elected. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified. A vacancy in the Board of Directors shall be deemed to exist under this Bylaw in the case of the death, removal or resignation of any director.

Section 19. Resignation. Any director may resign at any time by delivering his or her notice in writing or by electronic transmission to the Secretary, such resignation to specify whether it will be effective at a particular time, upon receipt by the Secretary or at the pleasure of the Board of Directors. If no such specification is made, it shall be deemed effective at the pleasure of the Board of Directors. When one or more directors shall resign from the Board of Directors, effective at a future date, a majority of the directors then in office, including those who have so resigned, shall have power to fill such vacancy or vacancies, the vote thereon to take effect when such resignation or resignations shall become effective, and each Director so chosen shall hold office for the unexpired portion of the term of the Director whose place shall be vacated and until his or her successor shall have been duly elected and qualified.

Section 20. Removal. Subject to any limitations imposed by applicable law, the Board of Directors or any director may be removed from office at any time (i) with cause by the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of capital stock of the corporation entitled to vote generally at an election of directors or (ii) without cause by the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of capital stock of the corporation, entitled to elect such director.

Section 21. Meetings

(a) Regular Meetings. Unless otherwise restricted by the Certificate of Incorporation, regular meetings of the Board of Directors may be held at any time or date and at any place within or without the State of Delaware which has been designated by the Board of Directors and publicized among all directors, either orally or in writing, including

a voice-messaging system or other system designated to record and communicate messages, facsimile, or by electronic mail or other electronic means. No further notice shall be required for a regular meeting of the Board of Directors.

(b) Special Meetings. Unless otherwise restricted by the Certificate of Incorporation, special meetings of the Board of Directors may be held at any time and place within or without the State of Delaware whenever called by the Chairman of the Board, the Chief Executive Officer (if a director), the President (if a director) or any two of the directors.

(c) Meetings by Electronic Communications Equipment. Any member of the Board of Directors, or of any committee thereof, may participate in a meeting by means of conference telephone or other communications equipment by means of which all persons participating in the meeting can hear each other, and participation in a meeting by such means shall constitute presence in person at such meeting.

(d) Notice of Special Meetings. Notice of the time and place of all special meetings of the Board of Directors shall be orally or in writing, by telephone, including a voice messaging system or other system or technology designed to record and communicate messages, facsimile, telegraph or telex, or by electronic mail or other electronic means, during normal business hours, at least 24 hours before the date and time of the meeting. If notice is sent by US mail, it shall be sent by first class mail, postage prepaid at least three days before the date of the meeting. Notice of any meeting may be waived in writing or by electronic transmission at any time before or after the meeting and will be waived by any director by attendance thereat, except when the director attends the meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

(e) Waiver of Notice. The transaction of all business at any meeting of the Board of Directors, or any committee thereof, however called or noticed, or wherever held, shall be as valid as though had at a meeting duly held after regular call and notice, if a quorum be present and if, either before or after the meeting, each of the directors not present who did not receive notice shall sign a written waiver of notice or shall waive notice by electronic transmission. All such waivers shall be filed with the corporate records or made a part of the minutes of the meeting.

Section 22. Quorum and Voting.

(a) Unless the Certificate of Incorporation requires a greater number, a quorum of the Board of Directors shall consist of a majority of the total number of directors then serving; *provided, however*, that such number shall never be less than 1/3 of the total number of directors except that when one director is authorized, then one director shall constitute a quorum. At any meeting, whether a quorum be present or otherwise, a majority of the directors present may adjourn from time to time until the time fixed for the next regular meeting of the Board of Directors, without notice other than by announcement at the meeting. If the Certificate of Incorporation provides that one or more directors shall have more or less than one vote per director on any matter, every reference in this Section to a majority or other proportion of the directors shall refer to a majority or other proportion of the votes of the directors.

(b) At each meeting of the Board of Directors at which a quorum is present, all questions and business shall be determined by the affirmative vote of a majority of the directors present, unless a different vote be required by law, the Certificate of Incorporation or these Bylaws.

Section 23. Action Without Meeting. Unless otherwise restricted by the Certificate of Incorporation or these Bylaws, any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting, if all members of the Board of Directors or committee, as the case may be, consent thereto in writing or by electronic transmission, and such writing or writings or transmission or transmissions are filed with the minutes of proceedings of the Board of Directors or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

Section 24. Fees and Compensation. Directors shall be entitled to such compensation for their services as may be approved by the Board of Directors, including, if so approved, by resolution of the Board of Directors, a fixed sum and expenses of attendance, if any, for attendance at each regular or special meeting of the Board of Directors and at any meeting of a committee of the Board of Directors. Nothing herein contained shall be construed to preclude any director from serving the corporation in any other capacity as an officer, agent, employee, or otherwise and receiving compensation therefor.

Section 25. Committees.

(a) Executive Committee. The Board of Directors may appoint an Executive Committee to consist of one or more members of the Board of Directors. The Executive Committee, to the extent permitted by law and provided in the resolution of the Board of Directors, shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation, and may authorize the seal of the corporation to be affixed to all papers which may require it; but no such committee shall have the power or authority in reference to (i) approving or adopting, or recommending to the stockholders, any action or matter expressly required by the DGCL to be submitted to stockholders for approval, or (ii) adopting, amending or repealing any bylaw of the corporation.

(b) Other Committees. The Board of Directors may, from time to time, appoint such other committees as may be permitted by law. Such other committees appointed by the Board of Directors shall consist of one or more members of the Board of Directors and shall have such powers and perform such duties as may be prescribed by the resolution or resolutions creating such committees, but in no event shall any such committee have the powers denied to the Executive Committee in these Bylaws.

(c) Term. The Board of Directors, subject to any requirements of any outstanding series of Preferred Stock and the provisions of paragraphs (a) or (b) of this Section may at any time increase or decrease the number of members of a committee or terminate the existence of a committee. The membership of a committee member shall terminate on the date of his or her death or voluntary resignation from the committee or from the Board of Directors. The Board of Directors may at any time for any reason remove any individual committee member and the Board of Directors may fill any committee vacancy created by death, resignation, removal or increase in the number of members of the committee. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee, and, in addition, in the absence or disqualification of any member of a committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not he or they constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of any such absent or disqualified member.

(d) Meetings. Unless the Board of Directors shall otherwise provide, regular meetings of the Executive Committee or any other committee appointed pursuant to this Section shall be held at such times and places as are determined by the Board of Directors, or by any such committee, and when notice thereof has been given to each member of such committee, no further notice of such regular meetings need be given thereafter. Special meetings of any such committee may be held at any place which has been determined from time to time by such committee, and may be called by any director who is a member of such committee, upon notice to the members of such committee of the time and place of such special meeting given in the manner provided for the giving of notice to members of the Board of Directors of the time and place of special meetings of the Board of Directors. Notice of any special meeting of any committee may be waived in writing at any time before or after the meeting and will be waived by any director by attendance thereat, except when the director attends such special meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Unless otherwise provided by the Board of Directors in the resolutions authorizing the creation of the committee, a majority of the authorized number of members of any such committee shall constitute a quorum for the transaction of business, and the act of a majority of those present at any meeting at which a quorum is present shall be the act of such committee.

Section 26. Organization. At every meeting of the directors, the Chairman of the Board of Directors, or, if a Chairman has not been appointed or is absent, the Chief Executive Officer (if a director), or if the Chief Executive Officer is not a director or is absent, the President (if a director), or if the President is not a director or is absent, the most senior Vice President (if a director) or, in the absence of any such person, a chairman of the meeting chosen by a majority of the directors present, shall preside over the meeting. The Secretary, or in his or her absence, any Assistant Secretary directed to do so by the Chief Executive Officer or President, shall act as secretary of the meeting.

ARTICLE V

OFFICERS

Section 27. Officers Designated. The officers of the corporation shall include, if and when designated by the Board of Directors, the Chief Executive Officer, the President, one or more Vice Presidents, the Secretary, the Chief Financial Officer, the Treasurer and the Controller, all of whom shall be elected at the annual organizational meeting of the Board of Directors. The Board of Directors may also appoint one or more Assistant Secretaries, Assistant Treasurers, Assistant Controllers and such other officers and agents with such powers and duties as it shall deem necessary. The Board of Directors may assign such additional titles to one or more of the officers as it shall deem appropriate. Any one person may hold any number of offices of the corporation at any one time unless specifically prohibited therefrom by law. The salaries and other compensation of the officers of the corporation shall be fixed by or in the manner designated by the Board of Directors.

Section 28. Tenure and Duties of Officers.

(a) General. All officers shall hold office at the pleasure of the Board of Directors and until their successors shall have been duly elected and qualified, unless sooner removed. Any officer elected or appointed by the Board of Directors may be removed at any time by the Board of Directors. If the office of any officer becomes vacant for any reason, the vacancy may be filled by the Board of Directors, or by the Chief Executive Officer or other officer if so authorized by the Board of Directors.

(b) Duties of Chairman of the Board of Directors. The Chairman of the Board of Directors, when present, shall preside at all meetings of the stockholders and the Board of Directors. The Chairman of the Board of Directors shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time. If there is no Chief Executive Officer and no President, then the Chairman of the Board of Directors shall also serve as the Chief Executive Officer of the corporation and shall have the powers and duties prescribed in paragraph (c) of this Section.

(c) Duties of Chief Executive Officer. The Chief Executive Officer shall preside at all meetings of the stockholders and (if a director) at all meetings of the Board of Directors, unless the Chairman of the Board of Directors has been appointed and is present. The Chief Executive Officer shall be the chief executive officer of the corporation and shall, subject to the control of the Board of Directors, have general supervision, direction and control of the business and officers of the corporation. The Chief Executive Officer shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time.

(d) Duties of President. In the absence or disability of the Chief Executive Officer or if the office of Chief Executive Officer is vacant, the President shall preside at all meetings of the stockholders and (if a director) at all meetings of the Board of Directors, unless the Chairman of the Board of Directors has been appointed and is present. If the office of Chief Executive Officer is vacant, the President shall be the chief executive officer of the corporation and shall, subject to the control of the Board of Directors, have general supervision, direction and control of the business and officers of the corporation. The President shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time.

(e) Duties of Vice Presidents. The Vice Presidents may assume and perform the duties of the President in the absence or disability of the President or whenever the office of President is vacant. The Vice Presidents shall perform other duties commonly incident to their office and shall also perform such other duties and have such other powers as the Board of Directors or the President shall designate from time to time.

(f) Duties of Secretary. The Secretary shall attend all meetings of the stockholders and of the Board of Directors and shall record all acts and proceedings thereof in the minute book of the corporation. The Secretary shall give notice in conformity with these Bylaws of all meetings of the stockholders and of all meetings of the Board of Directors and any committee thereof requiring notice. The Secretary shall perform all other duties provided for in these Bylaws and other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time. The Chief Executive Officer may direct any Assistant Secretary to

assume and perform the duties of the Secretary in the absence or disability of the Secretary, and each Assistant Secretary shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors or the Chief Executive Officer shall designate from time to time.

(g) Duties of Chief Financial Officer. The Chief Financial Officer shall keep or cause to be kept the books of account of the corporation in a thorough and proper manner and shall render statements of the financial affairs of the corporation in such form and as often as required by the Board of Directors or the Chief Executive Officer. The Chief Financial Officer, subject to the order of the Board of Directors, shall have the custody of all funds and securities of the corporation. The Chief Financial Officer shall perform other duties commonly incident to his or her office and shall also perform such other duties and have such other powers as the Board of Directors or the Chief Executive Officer shall designate from time to time. The Chief Executive Officer may direct the Treasurer or any Assistant Treasurer, or the Controller or any Assistant Controller to assume and perform the duties of the Chief Financial Officer in the absence or disability of the Chief Financial Officer, and each Treasurer and Assistant Treasurer and each Controller and Assistant Controller shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors or the Chief Executive Officer shall designate from time to time.

Section 29. Delegation of Authority. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

Section 30. Resignations. Any officer may resign at any time by giving notice in writing or by electronic transmission notice to the Board of Directors or to the Chief Executive Officer or to the President or to the Secretary. Any such resignation shall be effective when received by the person or persons to whom such notice is given, unless a later time is specified therein, in which event the resignation shall become effective at such later time. Unless otherwise specified in such notice, the acceptance of any such resignation shall not be necessary to make it effective. Any resignation shall be without prejudice to the rights, if any, of the corporation under any contract with the resigning officer.

Section 31. Removal. Any officer may be removed from office at any time, either with or without cause, by the affirmative vote of a majority of the directors in office at the time, or by the unanimous written or electronic consent of the directors in office at the time, or by any committee or superior officers upon whom such power of removal may have been conferred by the Board of Directors.

ARTICLE VI

EXECUTION OF CORPORATE INSTRUMENTS AND VOTING OF SECURITIES OWNED BY THE CORPORATION

Section 32. Execution of Corporate Instruments. The Board of Directors may, in its discretion, determine the method and designate the signatory officer or officers, or other person or persons, to execute on behalf of the corporation any corporate instrument or document, or to sign on behalf of the corporation the corporate name, or to enter into contracts on behalf of the corporation, except where otherwise provided by law or these Bylaws, and such execution or signature shall be binding upon the corporation.

All checks and drafts drawn on banks or other depositaries of funds to the credit of the corporation or on special accounts of the corporation shall be signed by such person or persons as the Board of Directors shall authorize so to do.

Unless authorized or ratified by the Board of Directors or within the agency power of an officer, no officer, agent or employee shall have any power or authority to bind the corporation by any contract or engagement or to pledge its credit or to render it liable for any purpose or for any amount.

Section 33. Voting of Securities Owned by the Corporation. All stock and other securities of other corporations owned or held by the corporation for itself, or for other parties in any capacity, shall be voted, and all proxies with respect thereto shall be executed, by the person authorized so to do by resolution of the Board of Directors, or, in the absence of such authorization, by the Chairman of the Board of Directors, the Chief Executive Officer, the President, or any Vice President.

ARTICLE VII

SHARES OF STOCK

Section 34. Form and Execution of Certificates. The shares of the corporation shall be represented by certificates, or shall be uncertificated. Certificates for the shares of stock, if any, of the corporation shall be in such form as is consistent with the Certificate of Incorporation and applicable law. Every holder of shares of stock in the corporation represented by certificate shall be entitled to have a certificate signed by or in the name of the corporation by the Chairman of the Board of Directors, the Chief Executive Officer, or the President or any Vice President and by the Treasurer or Assistant Treasurer or the Secretary or Assistant Secretary, certifying the number of shares owned by him or her in the corporation. Any or all of the signatures on the certificate may be facsimiles. In case any officer, transfer agent, or registrar who has signed or whose facsimile signature has been placed upon a certificate shall have ceased to be such officer, transfer agent, or registrar before such certificate is issued, it may be issued with the same effect as if he or she were such officer, transfer agent, or registrar at the date of issue.

Section 35. Lost Certificates. A new certificate or certificates shall be issued in place of any certificate or certificates theretofore issued by the corporation alleged to have been lost, stolen, or destroyed, upon the making of an affidavit of that fact by the person claiming the certificate of stock to be lost, stolen, or destroyed. The corporation may require, as a condition precedent to the issuance of a new certificate or certificates, the owner of such lost, stolen, or destroyed certificate or certificates, or the owner's legal representative, to agree to indemnify the corporation in such manner as it shall require or to give the corporation a surety bond in such form and amount as it may direct as indemnity against any claim that may be made against the corporation with respect to the certificate alleged to have been lost, stolen, or destroyed.

Section 36. Restrictions on Transfer.

(a) No holder of any of the shares of stock of the corporation may sell, transfer, assign, pledge, or otherwise dispose of or encumber any of the shares of stock of the corporation or any right or interest therein, whether voluntarily or by operation of law, or by gift or otherwise (each, a "***Transfer***") without the prior written consent of the corporation, upon duly authorized action of its Board of Directors. The corporation may withhold consent for any legitimate corporate purpose, as determined by the Board of Directors. Examples of the basis for the corporation to withhold its consent include, without limitation, (i) if such Transfer to individuals, companies or any other form of entity identified by the corporation as a potential competitor or considered by the corporation to be unfriendly; or (ii) if such Transfer increases the risk of the corporation having a class of security held of record by 2,000 or more persons, or 500 or more persons who are not accredited investors (as such term is defined by the SEC), as described in Section 12(g) of the 1934 Act and any related regulations, or otherwise requiring the corporation to register any class of securities under the 1934 Act; or (iii) if such Transfer would result in the loss of any federal or state securities law exemption relied upon by the corporation in connection with the initial issuance of such shares or the issuance of any other securities; or (iv) if such Transfer is facilitated in any manner by any public posting, message board, trading portal, internet site, or similar method of communication, including without limitation any trading portal or internet site intended to facilitate secondary transfers of securities; or (v) if such Transfer is to be effected in a brokered transaction; or (vi) if such Transfer represents a Transfer of less than all of the shares then held by the stockholder and its affiliates or is to be made to more than a single transferee.

(b) If a stockholder desires to Transfer any shares, then the stockholder shall first give written notice thereof to the corporation. The notice shall name the proposed transferee and state the number of shares to be transferred, the proposed consideration, and all other terms and conditions of the proposed transfer. Any shares proposed to be transferred to which Transfer the corporation has consented pursuant to paragraph (a) of this Section will first be subject to the corporation's right of first refusal located in Section 37 of these Bylaws.

(c) Any Transfer, or purported Transfer, of shares not made in strict compliance with this Section shall be null and void, shall not be recorded on the books of the corporation and shall not be recognized by the corporation.

(d) The foregoing restriction on Transfer shall terminate upon the date securities of the corporation are first offered to the public pursuant to a registration statement filed with, and declared effective by, the SEC under the Securities Act of 1933, as amended (the "***1933 Act***").

(e) The certificates representing shares of stock of the corporation shall bear on their face the following legend so long as the foregoing Transfer restrictions are in effect:

> "THE SHARES REPRESENTED BY THIS CERTIFICATE ARE SUBJECT TO A TRANSFER RESTRICTION, AS PROVIDED IN THE BYLAWS OF THE CORPORATION."

Section 37. Right of First Refusal. No stockholder shall Transfer any of the shares of stock of the corporation, except by a Transfer which meets the requirements set forth in this Section 37, in addition to any other restrictions or requirements set forth under applicable law or these Bylaws:

(a) If the stockholder desires to Transfer any of his or her shares of stock, then the stockholder shall first give written notice thereof to the corporation. The notice shall name the proposed transferee and state the number of shares to be transferred, the proposed consideration, and all other terms and conditions of the proposed transfer.

(b) For 30 days following receipt of such notice, the corporation shall have the option to purchase up to all the shares specified in the notice at the price and upon the terms set forth in such notice; *provided, however,* that, with the consent of the stockholder, the corporation shall have the option to purchase a lesser portion of the shares specified in said notice at the price and upon the terms set forth therein. In the event of a gift, property settlement or other Transfer in which the proposed transferee is not paying the full price for the shares, and that is not otherwise exempted from the provisions of this Section, the price shall be deemed to be the fair market value of the stock at such time as determined in good faith by the Board of Directors. In the event the corporation elects to purchase all of the shares or, with consent of the stockholder, a lesser portion of the shares, it shall give written notice to the transferring stockholder of its election and settlement for said shares shall be made as provided below in paragraph (d) of this Section.

(c) The corporation may assign its rights hereunder.

(d) In the event the corporation and/or its assignee(s) elect to acquire any of the shares of the transferring stockholder as specified in said transferring stockholder's notice, the Secretary of the corporation shall so notify the transferring stockholder and settlement thereof shall be made in cash within 30 days after the Secretary of the corporation receives said transferring stockholder's notice; provided that if the terms of payment set forth in said transferring stockholder's notice were other than cash against delivery, the corporation and/or its assignee(s) shall pay for said shares on the same terms and conditions set forth in said transferring stockholder's notice.

(e) In the event the corporation and/or its assignees(s) do not elect to acquire all of the shares specified in the transferring stockholder's notice, said transferring stockholder may, subject to the corporation's approval and all other restrictions on Transfer located in Section 36 of these Bylaws, within the 60-day period following the expiration or waiver of the option rights granted to the corporation and/or its assignees(s) herein, Transfer the shares specified in said transferring stockholder's notice which were not acquired by the corporation and/or its assignees(s) as specified in said transferring stockholder's notice. All shares so sold by said transferring stockholder shall continue to be subject to the provisions of this Bylaw in the same manner as before said Transfer.

(f) Anything to the contrary contained herein notwithstanding, the following transactions shall be exempt from the right of first refusal in paragraph (a) of this Section:

(1) A stockholder's Transfer of any or all shares held either during such stockholder's lifetime or on death by will or intestacy to such stockholder's immediate family or to any custodian or trustee for the account of such stockholder or such stockholder's immediate family or to any limited partnership of which the stockholder, members of such stockholder's immediate family or any trust for the account of such stockholder or such stockholder's immediate family will be the general or limited partner(s) of such partnership. "Immediate family" as used herein shall mean spouse, lineal descendant, father, mother, brother, or sister of the stockholder making such Transfer;

(2) A stockholder's bona fide pledge or mortgage of any shares with a commercial lending institution, provided that any subsequent Transfer of said shares by said institution shall be conducted in the manner set forth in this Bylaw;

(3) A stockholder's Transfer of any or all of such stockholder's shares to the corporation or to any other stockholder of the corporation;

(4) A stockholder's Transfer of any or all of such stockholder's shares to a person who, at the time of such Transfer, is an officer or director of the corporation;

(5) A corporate stockholder's Transfer of any or all of its shares pursuant to and in accordance with the terms of any merger, consolidation, reclassification of shares or capital reorganization of the corporate stockholder, or pursuant to a sale of all or substantially all of the stock or assets of a corporate stockholder;

(6) A corporate stockholder's Transfer of any or all of its shares to any or all of its stockholders; or

(7) A Transfer by a stockholder which is a limited or general partnership to any or all of its partners or former partners in accordance with partnership interests.

In any such case, the transferee, assignee, or other recipient shall receive and hold such stock subject to the provisions of this Section and any other restrictions set forth in these Bylaws, and there shall be no further Transfer of such stock except in accord with this Section and the other provisions of these Bylaws.

(g) The provisions of this Bylaw may be waived with respect to any Transfer either by the corporation, upon duly authorized action of its Board of Directors, or by the stockholders, upon the express written consent of the owners of a majority of the voting power of the corporation (excluding the votes represented by those shares to be transferred by the transferring stockholder). This Bylaw may be amended or repealed either by a duly authorized action of the Board of Directors or by the stockholders, upon the express written consent of the owners of a majority of the voting power of the corporation.

(h) Any Transfer, or purported Transfer, of securities of the corporation shall be null and void unless the terms, conditions, and provisions of this Bylaw are strictly observed and followed.

(i) The foregoing right of first refusal shall terminate upon the date securities of the corporation are first offered to the public pursuant to a registration statement filed with, and declared effective by, the SEC under the Securities Act of 1933, as amended.

(j) The certificates representing shares of stock of the corporation that are subject to the right of first refusal in paragraph (a) of this Section shall bear on their face the following legend so long as the foregoing right of first refusal remains in effect:

"THE SHARES REPRESENTED BY THIS CERTIFICATE ARE
SUBJECT TO A RIGHT OF FIRST REFUSAL OPTION IN FAVOR
OF THE CORPORATION AND/OR ITS ASSIGNEE(S), AS
PROVIDED IN THE BYLAWS OF THE CORPORATION."

(k) To the extent this Section conflicts with any written agreements between the Company and the stockholder attempting to Transfer shares, such agreement shall control.

Section 38. Fixing Record Dates.

(a) In order that the corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, the Board of Directors may fix, in advance, a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date shall, subject to applicable law, not be more than 60 nor less than 10 days before the date of such meeting. If no record date is fixed by the Board of Directors, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day immediately preceding the day on which notice is given, or if notice is waived, at the close of business on the day immediately preceding the day on which the meeting is

held. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; *provided, however,* that the Board of Directors may fix a new record date for the adjourned meeting.

(b) In order that the corporation may determine the stockholders entitled to consent to corporate action in writing without a meeting, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which date shall not be more than 10 days after the date upon which the resolution fixing the record date is adopted by the Board of Directors. Any stockholder of record seeking to have the stockholders authorize or take corporate action by written consent shall, by written notice to the Secretary, request the Board of Directors to fix a record date. The Board of Directors shall promptly, but in all events within 10 days after the date on which such a request is received, adopt a resolution fixing the record date. If no record date has been fixed by the Board of Directors within 10 days of the date on which such a request is received, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting, when no prior action by the Board of Directors is required by applicable law, shall be the first date on which a signed written consent setting forth the action taken or proposed to be taken is delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to the corporation's registered office shall be by hand or by certified or registered mail, return receipt requested. If no record date has been fixed by the Board of Directors and prior action by the Board of Directors is required by law, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting shall be at the close of business on the day on which the Board of Directors adopts the resolution taking such prior action.

(c) In order that the corporation may determine the stockholders entitled to receive payment of any dividend or other distribution or allotment of any rights or the stockholders entitled to exercise any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action, the Board of Directors may fix, in advance, a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted, and which record date shall be not more than 60 days prior to such action. If no record date is fixed, the record date for determining stockholders for any such purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto.

Section 39. Registered Stockholders. The corporation shall be entitled to recognize the exclusive right of a person registered on its books as the owner of shares to receive dividends, and to vote as such owner, and shall not be bound to recognize any equitable or other claim to or interest in such share or shares on the part of any other person whether or not it shall have express or other notice thereof, except as otherwise provided by the laws of Delaware.

ARTICLE VIII

OTHER SECURITIES OF THE CORPORATION

Section 40. Execution of Other Securities. All bonds, debentures and other corporate securities of the corporation, other than stock certificates (covered in Section 34 of these Bylaws), may be signed by the Chairman of the Board of Directors, the Chief Executive Officer, the President or any Vice President, or such other person as may be authorized by the Board of Directors, and the corporate seal impressed thereon or a facsimile of such seal imprinted thereon and attested by the signature of the Secretary or an Assistant Secretary, or the Chief Financial Officer or Treasurer or an Assistant Treasurer; *provided, however,* that where any such bond, debenture or other corporate security shall be authenticated by the manual signature, or where permissible facsimile signature, of a trustee under an indenture pursuant to which such bond, debenture or other corporate security shall be issued, the signatures of the persons signing and attesting the corporate seal on such bond, debenture or other corporate security may be the imprinted facsimile of the signatures of such persons. Interest coupons appertaining to any such bond, debenture or other corporate security, authenticated by a trustee as aforesaid, shall be signed by the Treasurer or an Assistant Treasurer of the corporation or such other person as may be authorized by the Board of Directors, or bear imprinted thereon the facsimile signature of such person. In case any officer who shall have signed or attested any bond, debenture or other corporate security, or whose facsimile signature shall appear thereon or on any such interest coupon, shall have ceased to be such officer before the bond, debenture or other corporate security so signed or attested shall have been delivered, such bond, debenture or other corporate security nevertheless may be adopted by the corporation and issued and delivered as though the person who signed the same or whose facsimile signature shall have been used thereon had not ceased to be such officer of the corporation.

ARTICLE IX

DIVIDENDS

Section 41. Declaration of Dividends. Dividends upon the capital stock of the corporation, subject to the provisions of the Certificate of Incorporation and applicable law, if any, may be declared by the Board of Directors pursuant to law at any regular or special meeting. Dividends may be paid in cash, in property, or in shares of the capital stock, subject to the provisions of the Certificate of Incorporation and applicable law.

Section 42. Dividend Reserve. Before payment of any dividend, there may be set aside out of any funds of the corporation available for dividends such sum or sums as the Board of Directors from time to time, in their absolute discretion, think proper as a reserve or reserves to meet contingencies, or for equalizing dividends, or for repairing or maintaining any property of the corporation, or for such other purpose as the Board of Directors shall think conducive to the interests of the corporation, and the Board of Directors may modify or abolish any such reserve in the manner in which it was created.

ARTICLE X

FISCAL YEAR

Section 43. Fiscal Year. The fiscal year of the corporation shall be fixed by resolution of the Board of Directors.

ARTICLE XI

INDEMNIFICATION

Section 44. Indemnification of Directors, Executive Officers, Other Officers, Employees and Other Agents.

(a) Directors and Executive Officers. The corporation shall indemnify its directors and executive officers (for the purposes of this Article, "executive officers" shall have the meaning defined in Rule 3b-7 promulgated under the 1934 Act) to the fullest extent not prohibited by the DGCL or any other applicable law; *provided, however,* that the corporation may modify the extent of such indemnification by individual contracts with its directors and executive officers; and, *provided, further,*

that the corporation shall not be required to indemnify any director or executive officer in connection with any proceeding (or part thereof) initiated by such person unless (i) such indemnification is expressly required to be made by law, (ii) the proceeding was authorized by the Board of Directors of the corporation, (iii) such indemnification is provided by the corporation, in its sole discretion, pursuant to the powers vested in the corporation under the DGCL or any other applicable law or (iv) such indemnification is required to be made under paragraph (d) of this Section.

(b) Other Officers, Employees and Other Agents. The corporation shall have power to indemnify its other officers, employees and other agents as set forth in the DGCL or any other applicable law. The Board of Directors shall have the power to delegate the determination of whether indemnification shall be given to any such person except executive officers to such officers or other persons as the Board of Directors shall determine.

(c) Expenses. The corporation shall advance to any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that such person is or was a director or executive officer of the corporation, or is or was serving at the request of the corporation as a director or executive officer of another corporation, partnership, joint venture, trust or other enterprise, prior to the final disposition of the proceeding, promptly following request therefor, all expenses incurred by any director or executive officer in connection with such proceeding, *provided, however*, that, if the DGCL requires, an advancement of expenses incurred by a director or officer in his or her capacity as a director or officer (and not in any other capacity in which service was or is rendered by such indemnitee, including, without limitation, service to an employee benefit plan) shall be made only upon delivery to the corporation of an undertaking, by or on behalf of such

indemnitee, to repay all amounts so advanced if it shall ultimately be determined by final judicial decision from which there is no further right to appeal that such indemnitee is not entitled to be indemnified for such expenses under this Section or otherwise.

Notwithstanding the foregoing, unless otherwise determined pursuant to paragraph (e) of this Section, no advance shall be made by the corporation to an executive officer of the corporation (except by reason of the fact that such executive officer is or was a director of the corporation, in which event this paragraph shall not apply) in any action, suit or proceeding, whether civil, criminal, administrative or investigative, if a determination is reasonably and promptly made (i) by a majority vote of a quorum consisting of directors who were not parties to the proceeding, even if not a quorum, or (ii) by a committee of such directors designated by a majority of such directors, even though less than a quorum, or (iii) if there are no such directors, or such directors so direct, by independent legal counsel in a written opinion, that the facts known to the decision-making party at the time such determination is made demonstrate clearly and convincingly that such person acted in bad faith or in a manner that such person did not believe to be in or not opposed to the best interests of the corporation.

(d) Enforcement. Without the necessity of entering into an express contract, all rights to indemnification and advances to directors and executive officers under this Section shall be deemed to be contractual rights and be effective to the same extent and as if provided for in a contract between the corporation and the director or executive officer. Any right to indemnification or advances granted by this Section to a director or executive officer shall be enforceable by or on behalf of the person holding such right in any court of competent jurisdiction if (i) the claim for indemnification or advances is denied, in whole or in part, or (ii) no disposition of such claim is made within 90 days of request therefor. The claimant in such enforcement action, if successful in whole or in part, shall be entitled to be paid also the expense of prosecuting the claim. In connection with any claim for indemnification, the corporation shall be entitled to raise as a defense to any such action that the claimant has not met the standards of conduct that make it permissible under the DGCL or any other applicable law for the corporation to indemnify the claimant for the amount claimed. In connection with any claim by an executive officer of the corporation (except in any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that such executive officer is or was a director of the corporation) for advances, the corporation shall be entitled to raise as a defense as to any such action clear and convincing evidence that such person acted in bad faith or in a manner that such person did not believe to be in or not opposed to the best interests of the corporation, or with respect to any criminal action or proceeding that such person acted without reasonable cause to believe that his or her conduct was lawful. Neither the failure of the corporation (including its Board of Directors, independent legal counsel or its stockholders) to have made a determination prior to the commencement of such action that indemnification of the claimant is proper in the circumstances because he has met the applicable standard of conduct set forth in the DGCL or any other applicable law, nor an actual determination by the corporation (including its Board of Directors, independent legal counsel or its stockholders) that the claimant has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that claimant has not met the applicable standard of conduct.

(e) Non-Exclusivity of Rights. The rights conferred on any person by this Section shall not be exclusive of any other right which such person may have or hereafter acquire under any applicable statute, provision of the Certificate of Incorporation, Bylaws, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his or her official capacity and as to action in another capacity while holding office. The corporation is specifically authorized to enter into individual contracts with any or all of its directors, officers, employees or agents respecting indemnification and advances, to the fullest extent not prohibited by the DGCL or any other applicable law.

(f) Survival of Rights. The rights conferred on any person by this Section shall continue as to a person who has ceased to be a director or executive officer and shall inure to the benefit of the heirs, executors and administrators of such a person.

(g) Insurance. To the fullest extent permitted by the DGCL, or any other applicable law, the corporation, upon approval by the Board of Directors, may purchase insurance on behalf of any person required or permitted to be indemnified pursuant to this Section.

(h) Amendments. Any repeal or modification of this Section shall only be prospective and shall not affect the rights under this Bylaw in effect at the time of the alleged occurrence of any action or omission to act that is the cause of any proceeding against any agent of the corporation.

(i) **Saving Clause**. If this Section or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the corporation shall nevertheless indemnify each director and executive officer to the full extent not prohibited by any applicable portion of this Bylaw that shall not have been invalidated, or by any other applicable law. If this Section shall be invalid due to the application of the indemnification provisions of another jurisdiction, then the corporation shall indemnify each director and executive officer to the full extent under applicable law.

(j) **Certain Definitions**. For the purposes of this Section, the following definitions shall apply:

(1) The term "proceeding" shall be broadly construed and shall include, without limitation, the investigation, preparation, prosecution, defense, settlement, arbitration and appeal of, and the giving of testimony in, any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative.

(2) The term "expenses" shall be broadly construed and shall include, without limitation, court costs, attorneys' fees, witness fees, fines, amounts paid in settlement or judgment and any other costs and expenses of any nature or kind incurred in connection with any proceeding.

(3) The term the "corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under the provisions of this Section with respect to the resulting or surviving corporation as he would have with respect to such constituent corporation if its separate existence had continued.

(4) References to a "director," "executive officer," "officer," "employee," or "agent" of the corporation shall include, without limitation, situations where such person is serving at the request of the corporation as, respectively, a director, executive officer, officer, employee, trustee or agent of another corporation, partnership, joint venture, trust or other enterprise.

(5) References to "other enterprises" shall include employee benefit plans; references to "fines" shall include any excise taxes assessed on a person with respect to an employee benefit plan; and references to "serving at the request of the corporation" shall include any service as a director, officer, employee or agent of the corporation which imposes duties on, or involves services by, such director, officer, employee, or agent with respect to an employee benefit plan, its participants, or beneficiaries; and a person who acted in good faith and in a manner he reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner "not opposed to the best interests of the corporation" as referred to in this Section.

ARTICLE XII

NOTICES

Section 45. **Notices**.

(a) **Notice to Stockholders**. Written notice to stockholders of stockholder meetings shall be given as provided in Section 7 of these Bylaws. Without limiting the manner by which notice may otherwise be given effectively to stockholders under any agreement or contract with such stockholder, and except as otherwise required by law, written notice to stockholders for purposes other than stockholder meetings may be sent by United States mail or nationally recognized overnight courier, or by facsimile, telegraph or telex or by electronic mail or other electronic means.

(b) **Notice to Directors**. Any notice required to be given to any director may be given by the method stated in paragraph (a) of this Section, or as provided for in Section 21 of these Bylaws. If such notice is not delivered personally, it shall be sent to such address as such director shall have filed in writing with the Secretary, or, in the absence of such filing, to the last known post office address of such director.

(c) Affidavit of Mailing. An affidavit of mailing, executed by a duly authorized and competent employee of the corporation or its transfer agent appointed with respect to the class of stock affected or other agent, specifying the name and address or the names and addresses of the stockholder or stockholders, or director or directors, to whom any such notice or notices was or were given, and the time and method of giving the same, shall in the absence of fraud, be prima facie evidence of the facts therein contained.

(d) Methods of Notice. It shall not be necessary that the same method of giving notice be employed in respect of all recipients of notice, but one permissible method may be employed in respect of any one or more, and any other permissible method or methods may be employed in respect of any other or others.

(e) Notice to Person with Whom Communication Is Unlawful. Whenever notice is required to be given, under any provision of law or of the Certificate of Incorporation or Bylaws of the corporation, to any person with whom communication is unlawful, the giving of such notice to such person shall not be required and there shall be no duty to apply to any governmental authority or agency for a license or permit to give such notice to such person. Any action or meeting which shall be taken or held without notice to any such person with whom communication is unlawful shall have the same force and effect as if such notice had been duly given. In the event that the action taken by the corporation is such as to require the filing of a certificate under any provision of the DGCL, the certificate shall state, if such is the fact and if notice is required, that notice was given to all persons entitled to receive notice except such persons with whom communication is unlawful.

(f) Notice to Stockholders Sharing an Address. Except as otherwise prohibited under DGCL, any notice given under the provisions of DGCL, the Certificate of Incorporation or the Bylaws shall be effective if given by a single written notice to stockholders who share an address if consented to by the stockholders at that address to whom such notice is given. Such consent shall have been deemed to have been given if such stockholder fails to object in writing to the corporation within 60 days of having been given notice by the corporation of its intention to send the single notice. Any consent shall be revocable by the stockholder by written notice to the corporation.

ARTICLE XIII

AMENDMENTS

Section 46. Amendments. The Board of Directors is expressly empowered to adopt, amend or repeal Bylaws of the corporation. The stockholders shall also have power to adopt, amend or repeal the Bylaws of the corporation; *provided, however*, that, in addition to any vote of the holders of any class or series of stock of the corporation required by law or by the Certificate of Incorporation, such action by stockholders shall require the affirmative vote of the holders of at least a majority of the voting power of all of the then-outstanding shares of the capital stock of the corporation entitled to vote generally in the election of directors, voting together as a single class.

ARTICLE XIV

LOANS TO OFFICERS

Section 47. Loans to Officers. Except as otherwise prohibited under applicable law, the corporation may lend money to, or guarantee any obligation of, or otherwise assist any officer or other employee of the corporation or of its subsidiaries, including any officer or employee who is a Director of the corporation or its subsidiaries, whenever, in the judgment of the Board of Directors, such loan, guarantee or assistance may reasonably be expected to benefit the corporation. The loan, guarantee or other assistance may be with or without interest and may be unsecured, or secured in such manner as the Board of Directors shall approve, including, without limitation, a pledge of shares of stock of the corporation. Nothing in these Bylaws shall be deemed to deny, limit or restrict the powers of guaranty or warranty of the corporation at common law or under any statute.

ARTICLE XV

MISCELLANEOUS

Section 48. **Forum**. Unless the corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of the corporation; (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the corporation to the corporation or the corporation's stockholders; (iii) any action asserting a claim against the corporation or any director or officer or other employee of the corporation arising pursuant to any provision of the DGCL, the certificate of incorporation or the Bylaws of the corporation; or (iv) any action asserting a claim against the corporation or any director or officer or other employee of the corporation governed by the internal affairs doctrine.

Exhibit 4.15

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

Iterum Therapeutics plc ("we", "us" or the "Company") has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"): our Ordinary Shares, $0.01 par value per share.

DESCRIPTION OF SHARE CAPITAL

The following description of our share capital is intended as a summary only and therefore is not a complete description of our share capital. This description is based upon, and is qualified by reference to, our Memorandum and Articles of Association (our "Constitution"), and applicable provisions of the Irish Companies Act 2014 (the "Irish Companies Act"). You should read our Constitution including our Articles of Association, which are filed as an exhibit to the Annual Report on Form 10-K of which this exhibit is a part, for the provisions that are important to you.

Capital Structure—Authorized Share Capital

Our authorized share capital consists of 300,000,000 ordinary shares of $0.01 each and 100,000,000 undesignated preferred shares of $0.01 each.

We may issue shares subject to the maximum authorized share capital contained in our Constitution. The authorized share capital may be increased or reduced (but not below the number of issued ordinary shares or preferred shares, as applicable) by a resolution approved by a simple majority of the votes of our shareholders cast at a general meeting (referred to under Irish law as an "ordinary resolution") (unless otherwise determined by the directors). The shares comprising our authorized share capital may be divided into shares of any nominal value.

The rights and restrictions to which the ordinary shares are subject are prescribed in our Articles of Association. Our Articles of Association entitle our board of directors, without shareholder approval, to determine the terms of our preferred shares. Preferred shares may be preferred as to dividends, rights upon liquidation or voting in such manner as our board of directors may resolve. The preferred shares may also be redeemable at the option of the holder of the preferred shares or at our option and may be convertible into or exchangeable for shares of any of our other class or classes, depending on the terms of such preferred shares.

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

Whenever an alteration or reorganization of our share capital would result in any of our shareholders becoming entitled to fractions of a share, our board of directors may, on behalf of those shareholders that would become entitled to fractions of a share, arrange for the sale of the shares representing fractions and the distribution of the net proceeds of sale in due proportion among the shareholders who would have been entitled to the fractions.

Issuance of Shares

As a matter of Irish law, the board of directors of a company may issue authorized but unissued new shares without shareholder approval once authorized to do so by the Articles of Association of the company or by an ordinary resolution adopted by the shareholders at a general meeting. The authority conferred can be granted for a maximum period of five years, at which point it must be renewed by the shareholders by an ordinary resolution. Our board of directors is authorized pursuant to a shareholder resolution passed on January 28, 2021 to issue new ordinary or preferred shares up to the amount of the authorized but unissued share capital at that date without shareholder approval, with such authority expiring on January 26, 2026.

Pre-emption Rights, Share Warrants and Share Options

Under Irish law certain statutory pre-emption rights apply automatically in favor of shareholders where shares, warrants, convertibleinstruments or options are to be issued for cash. However, we have opted out of these pre-emption rights by way of shareholder resolution passed on January 28, 2021 as permitted under Irish company law. Irish law requires this opt-out to be renewed every five years by a resolution approved by not less than 75% of the votes of our shareholders cast at a general meeting (referred to under Irish law as a "special resolution") and our current opt-out will expire on January 26, 2026. If the opt-out is not renewed, shares issued for cash must be offered to our existing shareholders on a *pro rata* basis to their existing shareholding before the shares can be issued to any new shareholders. The statutory pre-emption rights do not apply where shares are issued for non-cash consideration (such as in a share-for-share acquisition) and do not apply to the issue of non-equity shares (that is, shares that have the right to participate only up to a specified amount in any income or capital distribution) or where shares are issued pursuant to an employee share option or similar equity plan.

Our Articles of Association provide that, subject to any shareholder approval requirement under any laws, regulations or the rules of any stock exchange to which we are subject, the board of directors is authorized, from time to time, in its discretion, to grant such persons, for such periods and upon such terms as the board of directors deems advisable, options to purchase such number of shares of any class or classes or of any series of any class as the board of directors may deem advisable, and to cause warrants or other appropriate instruments evidencing such options to be issued. The Irish Companies Act provides that directors may issue share warrants or options without shareholder approval once authorized to do so by the Articles of Association. We are subject to the rules of the Nasdaq Capital Market that require shareholder approval of certain equity plans and share issuances. Our board of directors may authorize the issuance of shares upon exercise of warrants or options without shareholder approval or authorization (up to the relevant authorized share capital limit).

Under Irish law, we are prohibited from allotting shares without consideration. Accordingly, at least the nominal value of the shares issued underlying any restricted share award, restricted share unit, performance share award, bonus share or any other share based grant must be paid pursuant to the Irish Companies Act.

Dividends

Under Irish law, dividends and distributions may only be made from distributable reserves. Distributable reserves, broadly, means the accumulated realized profits of a company, so far as not previously utilized by distribution or capitalization, less accumulated realized losses of a company, so far as not previously written off in a reduction or reorganization of capital, and includes reserves created by way of capital reduction, on a standalone basis. In addition, no distribution or dividend may be made unless our net assets are equal to, or in excess of, the aggregate of our called up share capital plus undistributable reserves and the distribution does not reduce our net assets below such aggregate. Undistributable reserves include the undenominated capital, the amount by which our accumulated unrealized profits, so far as not previously utilized by any capitalization, exceed our accumulated unrealized losses, so far as not previously written off in a reduction or reorganization of capital and any other reserve that we are prohibited from distributing by applicable law.

The determination as to whether or not we have sufficient distributable reserves to fund a dividend must be made by reference to the "relevant financial statements" of the Company. The "relevant financial statements" are either the last set of unconsolidated annual audited financial statements or unaudited financial statements properly prepared in accordance with the Irish Companies Act, which give a "true and fair view" of the Company's unconsolidated financial position in accordance with accepted accounting practice in Ireland. The "relevant financial statements" must be filed in the Companies Registration Office (the official public registry for companies in Ireland) prior to the making of the distribution.

Consistent with Irish law, our Articles of Association authorize the directors to declare interim dividends without shareholder approval out of funds lawfully available for the purpose, to the extent they appear justified by profits and subject always to the requirement to have distributable reserves at least equal to the amount of the proposed dividend. The board of directors may also recommend a dividend to be approved and declared by our shareholders at a general meeting. The board of directors may direct that the payment be made by distribution of assets, shares or cash and no dividend declared or paid may exceed the amount recommended by the directors. Dividends may be paid in U.S. dollars or any other currency.

Our directors may deduct from any dividend payable to any shareholder any amounts payable by such shareholder to us in relation to our shares.

Our directors may also authorize the issuance of shares with preferred rights to participate in our declared dividends. The holders of preferred shares may, depending on their terms, rank senior to our ordinary shares in terms of dividend rights and/or be entitled to claim arrears of a declared dividend out of subsequently declared dividends in priority to ordinary shareholders.

Share Repurchases, Redemptions and Conversions

Overview

Our Articles of Association provide that, in general, any ordinary share which we have agreed to acquire shall be deemed to be a redeemable share. Accordingly, for Irish company law purposes, the repurchase of ordinary shares by us may technically be effected as a redemption of those shares as described below under "—Repurchases and Redemptions." If our Articles of Association did not contain such provisions, all repurchases by us would be subject to many of the same rules that apply to purchases of our shares by subsidiaries described below under "—Purchases by Subsidiaries" including the shareholder approval requirements described below. Except where otherwise noted, when we refer to repurchasing or buying back our ordinary shares, we are referring to the redemption of ordinary shares by us pursuant to the Articles of Association or the purchase of our ordinary shares by a subsidiary of the Company, in each case in accordance with our Articles of Association and Irish law as described below. Holders of our ordinary shares have no right to convert the shares into any other security.

Repurchases and Redemptions

Under Irish law, a company may issue redeemable shares and redeem them out of distributable reserves (which are described above under "Dividends") or, if the company proposes to cancel the shares on redemption, the proceeds of a new issue of shares for that purpose. The redemption of redeemable shares may only be made by us where the nominal value of the issued share capital that is not redeemable is not less than 10% of the nominal value of the total issued share capital of the company. All redeemable shares must also be fully-paid and the terms of redemption of the shares must provide for payment on redemption. Redeemable shares may, upon redemption, be cancelled or held in treasury. Based on the provisions of our articles described above, shareholder approval will not be required to redeem our shares.

We may also be given an additional general authority by our shareholders to purchase our own shares on-market, which would take effect on the same terms and be subject to the same conditions as applicable to purchases by our subsidiaries as described below.

Our board of directors may also issue preferred shares or other classes or series of shares which may be redeemed at either our option or the option of the shareholder, depending on the terms of such preferred shares. Please see "—Capital Structure—Authorized Share Capital."

Repurchased and redeemed shares may be cancelled or held as treasury shares. The nominal value of treasury shares held by us at any time must not exceed 10% of the nominal value of our issued share capital. We may not exercise any voting rights in respect of any shares held as treasury shares. Treasury shares may be cancelled by us or re-issued subject to certain conditions.

Purchases by Subsidiaries

Under Irish law, an Irish or non-Irish subsidiary of the Company may purchase our shares either as overseas market purchases on a recognized stock exchange such as the Nasdaq or off-market. For a subsidiary of ours to make market purchases of our shares, our shareholders must provide general authorization for such purchase by way of ordinary resolution. However, as long as this general authority has been granted, no specific shareholder authority for a particular market purchase by a subsidiary of our shares is required. We may elect to seek such general authority, which must expire no later than 18 months after the date on which it was granted, at our annual general meetings.

For an off-market purchase by a subsidiary of ours, the proposed purchase contract must be authorized by special resolution of the shareholders before the contract is entered into. The person whose shares are to be bought back cannot vote in favor of the special resolution and from the date of the notice of the meeting at which the resolution approving the contract is proposed, the purchase contract must be on display or must be available for inspection by shareholders at our registered office from the date of the notice of the meeting at which the resolution approving the contract is to be proposed.

In order for a subsidiary of ours to make an on-market purchase of our shares, such shares must be purchased on a "recognized stock exchange." The Nasdaq Capital Market, on which our ordinary shares are listed, is specified as a recognized stock exchange for this purpose by Irish company law.

The number of shares held by our subsidiaries at any time will count as treasury shares and will be included in any calculation of the permitted treasury share threshold of 10% of the nominal value of our issued share capital. While a subsidiary holds shares of ours, it cannot exercise any voting rights in respect of those shares. The acquisition of our shares by a subsidiary of ours must be funded out of distributable reserves of the subsidiary.

Lien on Shares, Calls on Shares and Forfeiture of Shares

Our Articles of Association provide that we will have a first and paramount lien on every share for all debts and liabilities of any shareholder to the Company, whether presently due or not, payable in respect of such share. Subject to the terms of their allotment, directors may call for any unpaid amounts in respect of any shares to be paid, and if payment is not made within 14 days after notice demanding payment, we may sell the shares. These provisions are standard inclusions in the Articles of Association of an Irish company limited by shares and will only be applicable to our shares that have not been fully paid up. See "—Transfer and Registration of Shares."

Consolidation and Division; Subdivision

Under our Articles of Association, we may, by ordinary resolution (unless the directors determine otherwise), divide all or any of our issued share capital into shares of smaller nominal value than our existing shares (often referred to as a share split) or consolidate all or any of our issued share capital into shares of larger nominal value than is fixed by our memorandum of association (often referred to as a reverse share split), provided that the proportion between the amount paid for such share and the amount, if any, unpaid on each reduced share after the subdivision remains the same.

Reduction of Share Capital

We may, by ordinary resolution (unless the directors determine otherwise), reduce our authorized but unissued share capital in any way. We also may, by special resolution and subject to confirmation by the Irish High Court, reduce or cancel our issued share capital in any manner permitted by the Irish Companies Act.

Annual General Meetings of Shareholders

We are required to hold an annual general meeting within 18 months of incorporation and at intervals of no more than 15 months thereafter, provided that an annual general meeting is held in each calendar year following the first annual general meeting and no more than nine months after our fiscal year-end. Any annual general meeting may be held outside Ireland, provided that technological means are provided to enable shareholders to participate in the meeting without leaving Ireland.

Notice of an annual general meeting must be given to all of our shareholders and to our auditors. Our Articles of Association provide for a minimum notice period of 21 clear days (i.e. 21 days excluding the day when the notice is given or deemed to be given and the day of the event for which it is given or on which it is to take effect), which is the minimum permitted under Irish law.

The only matters which must, as a matter of Irish company law, be transacted at an annual general meeting are (i) the consideration of the statutory financial statements, report of the directors, and report of the statutory auditors, (ii) review by the members of the company's affairs and (iii) the appointment or re-appointment of the statutory auditors.

At any annual general meeting, only such business may be conducted as has been brought before the meeting:

- in the notice of the meeting;
- by or at the direction of the board of directors;
- in certain circumstances, at the direction of the Irish High Court;
- as required by law; or
- that the chairman of the meeting determines is properly within the scope of the meeting.

In addition, and subject to compliance with our Articles of Association, shareholders entitled to vote at an annual general meeting may propose business in advance of the meeting to be considered thereat.

Extraordinary General Meetings of Shareholders

Our extraordinary general meetings may be convened by (i) the board of directors, (ii) on requisition of the shareholders holding not less than 10% of our paid up share capital carrying voting rights, (iii) in certain circumstances, on requisition of our auditors; or (iv) in exceptional cases, by order of the Irish High Court.

Extraordinary general meetings are generally held for the purpose of approving shareholder resolutions as may be required from time to time. At any extraordinary general meeting, only such business will be conducted as is set forth in the notice thereof or is proposed pursuant to and in accordance with the procedures and requirements set out in our Articles of Association.

Notice of an extraordinary general meeting must be given to all of our shareholders and to our auditors. Under Irish law and our Articles of Association, the minimum notice periods are 21 clear days' notice in writing for an extraordinary general meeting to approve a special resolution and 14 clear days' notice in writing for any other extraordinary general meeting.

In the case of an extraordinary general meeting convened by our shareholders, the proposed purpose of the meeting must be set out in the requisition notice. Upon receipt of any such valid requisition notice, our board of directors has 21 days to convene a meeting of our shareholders to vote on the matters set out in the requisition notice. This meeting must be held within two months of the receipt of the requisition notice. If the board of directors does not convene the meeting within such 21 day period, the requisitioning shareholders, or any of them representing more than one half of the total voting rights of all of them, may themselves convene a meeting, which meeting must be held within three months of our receipt of the requisition notice.

If the board of directors becomes aware that our net assets are not greater than half of the amount of our called-up share capital, our directors must convene an extraordinary general meeting of our shareholders not later than 28 days from the date that the fact is known to a director to be held not later than 56 days from such date. This meeting must be convened for the purposes of considering whether any, and if so what, measures should be taken to address the situation.

Quorum for General Meetings

Our Articles of Association provide that no business shall be transacted at any general meeting unless a quorum is present. One or more shareholders present in person or by proxy at any meeting of shareholders holding not less than a majority of the issued shares that carry the right to vote at the meeting constitutes a quorum for the conduct of any business at a general meeting.

Voting

Our Articles of Association provide that all votes at a general meeting will be decided on a poll and that the board or the chairman may determine the manner in which the poll is to be taken and the manner in which the votes are to be counted.

Every shareholder is entitled to one vote for each ordinary share that he or she holds as of the record date for the meeting. Voting rights may be exercised by shareholders registered in our share register as of the record date for the meeting or by a duly appointed proxy, which proxy need not be a shareholder. Where interests in shares are held by a nominee trust company, this company may exercise the rights of the beneficial holders on their behalf as their proxy. All proxies must be appointed in the manner prescribed by our Articles of Association, which provide that our board of directors may permit shareholders to notify us of their proxy appointments electronically.

In accordance with our Articles of Association, our directors may from time to time authorize the issuance of preferred shares or any other class or series of shares. These shares may have such voting rights as may be specified in the terms of such shares (e.g., they may carry more votes per share than ordinary shares or may entitle their holders to a class vote on such matters as may be satisfied in the terms of such shares). Treasury shares or shares of ours that are held by our subsidiaries will not be entitled to be voted at general meetings of shareholders.

Irish company law requires special resolutions of the shareholders at a general meeting to approve certain matters. Examples of matters requiring special resolutions include:

- amending the objects as contained in our memorandum of association;
- amending our Articles of Association;
- approving a change of name;
- authorizing the entering into of a guarantee or provision of security in connection with a loan, quasi-loan or credit; transaction to a director or connected person;
- opting out of pre-emption rights on the issuance of new shares;
- re-registration from a public limited company to a private company;
- purchase of own shares off-market;
- reduction of issued share capital;
- sanctioning a compromise/scheme of arrangement;
- resolving that the company be wound up by the Irish courts;
- resolving in favor of a shareholders' voluntary winding-up;
- re-designation of shares into different share classes;
- setting the re-issue price of treasury shares; and

- variation of class rights attaching to classes of shares (where our Articles of Association do not provide otherwise).

Neither Irish law nor any of our constituent documents places limitations on the right of non-resident or foreign owners to vote or hold our shares.

Variation of Rights Attaching to a Class or Series of Shares

Under our Articles of Association and the Irish Companies Act, any variation of class rights attaching to our issued shares must be approved by an ordinary resolution passed at a general meeting of the shareholders of the affected class or with the consent in writing of the holders of a majority of the issued shares of that class of shares entitled to vote on such variation. The rights conferred upon the holder of any pre-existing issued shares shall not be deemed to be varied by the issuance of any preferred shares.

The provisions of our Articles of Association relating to general meetings apply to general meetings of the holders of any class of shares except that the necessary quorum is determined in reference to the shares of the holders of the class. Accordingly, for general meetings of holders of a particular class of shares, a quorum consists of one or more shareholders present in person or by proxy holding not less than a majority of the issued and outstanding shares of the class entitled to vote at the meeting in question.

Record Date

Our Articles of Association provide that the board may fix in advance a date as the record date (i) for any such determination of members entitled to notice of or to vote at a general meeting of the members, which record date shall not be more than 60 days before the date of such meeting, and (ii) for the purpose of determining the members entitled to receive payment of any dividend or other distribution, or in order to make a determination of members for any other proper purpose, which record date shall not be more than 60 days prior to the date of payment of such dividend or other distribution or the taking of any action to which such determination of members is relevant.

If no record date is fixed for the determination of members entitled to notice of or to vote at a meeting of members, the date immediately preceding the date on which notice of the meeting is deemed given under our Articles of Association will be the record date for such determination of members.

Shareholder Proposals

Under Irish law, there is no general right for a shareholder to put items on the agenda of an annual general meeting of a U.S.-listed company, other than as set out in the Articles of Association of a company. Under our Articles of Association, in addition to any other applicable requirements, for business or nominations to be properly brought before an annual general meeting by a shareholder, such shareholder must have given timely notice thereof in proper written form to our corporate secretary.

To be timely for an annual general meeting, a shareholder's notice to our secretary as to the business or nominations to be brought before the meeting must be delivered to or mailed and received at our registered office (i) with respect to our first annual general meeting as a public limited company, not later than the 10th day following the day on which public announcement of the date of such annual general meeting is made and (ii) with respect to all other annual general meetings not less than 90 days nor more than 120 days before the first anniversary of the notice convening our annual general meeting for the prior year. In the event that the date of the annual general meeting is changed by more than 30 days from the first anniversary date of the preceding year's annual general meeting, notice by the member must be so delivered by close of business on the day that is not earlier than 120 days prior to such annual general meeting and not later than the close of business on the later of (a) 90 days prior to the day of the contemplated annual general meeting or (b) 10 days after the day on which public announcement of the date of the contemplated annual general meeting is first made by us. In no event shall the public announcement of an adjournment or postponement of an annual general meeting commence a new time period (or extend any time period) for the giving of a shareholder's notice.

To be timely for business or nominations of a director at an extraordinary general meeting, notice must be delivered, or mailed and received not less than 90 days nor more than 120 days prior to the date of such extraordinary general meeting or, if the first public announcement of the date of the extraordinary general meeting is less than 100 days prior to the date of the meeting, by close of business 10 days after the day on which the public announcement of the date of the extraordinary general meeting is first made by us.

For nominations to the board, the notice must include all information about the director nominee that is required to be disclosed by U.S. Securities and Exchange Commission rules regarding the solicitation of proxies for the election of directors pursuant to Regulation 14A under the Exchange Act. For other business that a shareholder proposes to bring before the meeting, the notice must include a brief description of the business, the reasons for proposing the business at the meeting and a discussion of any material interest of the shareholder in the business. Whether the notice relates to a nomination to the board of directors or to other business to be proposed at the meeting, the notice also must include information about the shareholder and the shareholder's holdings of our shares. The chairman of the meeting shall have the power and duty to determine whether any business proposed to be brought before the meeting was made or proposed in accordance with these procedures (as set out in our Articles of Association), and if any proposed business is not in compliance with these provisions, to declare that such defective proposal shall be disregarded.

Shareholders' Suits

In Ireland, the decision to institute proceedings on behalf of a company is generally taken by the company's board of directors. In certain limited circumstances, a shareholder may be entitled to bring a derivative action on our behalf. The central question at issue in deciding whether a minority shareholder may be permitted to bring a derivative action is whether, unless the action is brought, a wrong committed against us would otherwise go unredressed. The cause of action may be against a director, another person or both.

A shareholder may also bring proceedings against us in his or her own name where the shareholder's rights as such have been infringed or where our affairs are being conducted, or the powers of the board of directors are being exercised, in a manner oppressive to any shareholder or shareholders or in disregard of their interests as shareholders. Oppression connotes conduct that is burdensome, harsh or wrong. This is an Irish statutory remedy under Section 212 of the Irish Companies Act and the court can grant any order it sees fit, including providing for the purchase or transfer of the shares of any shareholder.

Inspection of Books and Records

Under Irish law, shareholders have the right to: (i) receive a copy of our Constitution; (ii) inspect and obtain copies of the minutes of general meetings and any resolutions; (iii) inspect and receive a copy of the register of shareholders, register of directors and secretaries, register of directors' interests and other statutory registers maintained by us; (iv) inspect copies of directors' service contracts; (v) inspect copies of instruments creating charges; (vi) receive copies of statutory financial statements and directors' and auditors' reports which have previously been sent to shareholders prior to an annual general meeting; and (vii) receive financial statements of a subsidiary company of ours which have previously been sent to shareholders prior to an annual general meeting for the preceding 10 years. Our auditors will also have the right to inspect all of our books, records and vouchers. The auditors' report must be circulated to the shareholders with our financial statements prepared in accordance with Irish law with the notice of annual general meeting and must be presented to our shareholders at our annual general meeting.

Acquisitions

There are a number of mechanisms for acquiring an Irish public limited company, including:

- a court-approved scheme of arrangement under the Irish Companies Act. A scheme of arrangement with one or more classes of shareholders requires a court order from the Irish High Court and the approval of (i) more than 50% in number of the shareholders of each participating class or series voting on the scheme of arrangement, and (ii) representing 75% in value of the shares of such participating class or series held by the shareholders voting on the scheme of arrangement, in each case at the relevant meeting or meetings. A scheme of arrangement, if authorized by the shareholder of each participating class or series and the court, is binding on all of the shareholders of each participating class or series;

- through a tender or takeover offer by a third party, in accordance with the Irish Takeover Rules and the Irish Companies Act, for all of our shares. Where the holders of 80% or more of our shares (excluding any shares already beneficially owned by the bidder) have accepted an offer for their shares, the remaining shareholders may also be statutorily required to transfer their shares, unless, within one month, the non-tendering shareholders can obtain an Irish court order otherwise providing. If the offeror has acquired acceptances of 80% of all of our shares but does not exercise its "squeeze-out" right, then the non-accepting shareholders also have a statutory right to require the bidder to acquire their shares on the same terms as the original offer, or such other terms as the bidder and the non-tendering shareholders may agree or on such term as an Irish court, on application of the bidder or non-tendering shareholder, may order. If our shares were to be listed on the Euronext Dublin or another regulated stock exchange in the European Union, the aforementioned 80% threshold would be increased to 90%;

- by way of a transaction with a company incorporated in the European Economic Area which includes all member states of the European Union and Norway, Iceland and Liechtenstein ("EEA") under the European Communities (Cross-Border Mergers) Regulations 2008 (as amended). Such a transaction must be approved by a special resolution and by the Irish High Court. If we are being merged with another EEA company under the EU Cross-Border Mergers Directive (EU) 2019/2121 and the consideration payable to our shareholders is not all in the form of cash, our shareholders may be entitled to require their shares to be acquired at fair value; and

- by way of a merger with another Irish company under the Irish Companies Act which must be approved by a special resolution and by the Irish High Court.

Appraisal Rights

Generally, under Irish law, shareholders of an Irish company do not have statutory appraisal rights. If we are being merged as the transferor company with another EEA company under the European Communities (Cross-Border Merger) Regulations 2008 (as amended) or if we are being merged with another Irish company under the Irish Companies Act, (i) any of our shareholders who voted against the special resolution approving the merger or (ii) if 90% of our shares are held by the successor company, any other of our shareholders, may be entitled to require that the successor company acquire its shares for cash.

Disclosure of Interests in Shares

Under the Irish Companies Act, there is a notification requirement for shareholders who acquire or cease to be interested in 3% of the shares of an Irish public limited company. Our shareholders must therefore make such a notification to us if, as a result of a transaction, the shareholder will become interested in 3% or more of our shares or if, as a result of a transaction, a shareholder who was interested in 3% or more of our shares ceases to be so interested. Where a shareholder is interested in 3% or more of our shares, the shareholder must notify us of any alteration of his or her interest that brings his or her total holding through the nearest whole percentage number, whether an increase or a reduction. The relevant percentage figure is calculated by reference to the aggregate nominal value of the shares in which the shareholder is interested as a proportion of the entire nominal value of our issued share capital (or any such class of share capital in issue). Where the percentage level of the shareholder's interest does not amount to a whole percentage, this figure may be rounded down to the next whole number. All such disclosures should be notified to us within five business days of the transaction or alteration of the shareholder's interests that gave rise to the notification requirement. If a shareholder fails to comply with these notification requirements, the shareholder's rights in respect of any of our shares it holds will not be enforceable, either directly or indirectly. However, such person may apply to the court to have the rights attaching to such shares reinstated.

In addition to these disclosure requirements, under the Irish Companies Act, we may by notice in writing, require a person whom we know or have reasonable cause to believe to be, or at any time during the three years immediately preceding the date on which such notice is issued to have been, interested in shares comprised in our relevant share capital to: (i) indicate whether or not it is the case and (ii) where such person holds or has during that time held an interest in our ordinary shares, to provide additional information, including the person's own past or present interests in our shares. If the recipient of the notice fails to respond within the reasonable time period specified in the notice, we may apply to court for an order directing that the affected shares be subject to certain restrictions, as prescribed by the Irish Companies Act, as follows:

- any transfer of those shares, or in the case of unissued shares any transfer of the right to be issued with shares and any issue of shares, will be void;
- no voting rights will be exercisable in respect of those shares;
- no further shares will be issued in right of those shares or in pursuance of any offer made to the holder of those shares; and
- no payment will be made of any sums due from us on those shares, whether in respect of capital or otherwise.

Where our shares are subject to these restrictions, the court may order the shares to be sold and may also direct that the shares shall cease to be subject to these restrictions.

In the event we are in an offer period pursuant to the Irish Takeover Rules, accelerated disclosure provisions apply for persons holding an interest in our securities of 1.0% or more.

Irish Takeover Rules

A transaction in which a third party seeks to acquire 30% or more of our voting rights will be governed by the Irish Takeover Panel Act 1997 and the Irish Takeover Rules made thereunder and will be regulated by the Irish Takeover Panel. The "General Principles" of the Irish Takeover Rules and certain important aspects of the Irish Takeover Rules are described below.

General Principles

The Irish Takeover Rules are built on the following General Principles, which will apply to any transaction regulated by the Irish Takeover Panel:

- in the event of an offer, all holders of securities of the target company should be afforded equivalent treatment and, if a person acquires control of a company, the other holders of securities must be protected;
- the holders of the securities in the target company must have sufficient time and information to enable them to reach a properly informed decision on the offer;
- where it advises the holders of securities, the board of the target company must give its views on the effects of implementation of the offer on employment, conditions of employment and the locations of the target company's places of business;
- the board of the target company must act in the interests of the company as a whole and must not deny the holders of securities the opportunity to decide on the merits of the offer;
- false markets must not be created in the securities of the target company, the bidder or of any other company concerned by the offer in such a way that the rise or fall of the prices of the securities becomes artificial and the normal functioning of the markets is distorted;

- a bidder must announce an offer only after ensuring that he or she can fulfil in full, any cash consideration, if such is offered, and after taking all reasonable measures to secure the implementation of any other type of consideration;

- a target company must not be hindered in the conduct of its affairs for longer than is reasonable by an offer for its securities; and
- a substantial acquisition of securities (whether such acquisition is to be effected by one transaction or a series of transactions) shall take place only at an acceptable speed and shall be subject to adequate and timely disclosure.

Mandatory Bid

Under certain circumstances, a person who acquires shares or other of our voting rights may be required under the Irish Takeover Rules to make a mandatory cash offer for our remaining outstanding shares at a price not less than the highest price paid for the shares by the acquirer (or any parties acting in concert with the acquirer) during the previous 12 months. This mandatory bid requirement is triggered if an acquisition of shares would (i) increase the aggregate holding of an acquirer (including the holdings of any parties acting in concert with the acquirer) to shares representing 30% or more of our voting rights, or (ii) in the case of a person holding (together with its concert parties) shares representing 30% or more of our voting rights, after giving effect to the acquisition, increase the percentage of the voting rights held by that person (together with its concert parties) by 0.05% within a 12-month period. Any person (excluding any parties acting in concert with the holder) holding shares representing more than 50% of the voting rights of a company is not subject to these mandatory offer requirements in purchasing additional securities.

Voluntary Bid; Requirements to Make a Cash Offer and Minimum Price Requirements

A voluntary offer is an offer that is not a mandatory offer. If a person makes a voluntary offer to acquire outstanding ordinary shares of ours, the offer price must be no less than the highest price paid for our shares by the bidder or its concert parties during the three-month period prior to the commencement of the offer period. The Irish Takeover Panel has the power to extend the "look back" period to 12 months if the Irish Takeover Panel, taking into account the General Principles, believes it is appropriate to do so.

If the bidder or any party acting in concert with it has acquired our ordinary shares (i) during the period of 12 months prior to the commencement of the offer period which represent more than 10% of our total ordinary shares or (ii) at any time after the commencement of the offer period, the offer must be in cash (or accompanied by a full cash alternative) and the price per ordinary share must not be less than the highest price paid by the bidder or any party acting in concert with it during, in the case of (i), the 12-month period prior to the commencement of the offer period and, in the case of (ii), the offer period. The Irish Takeover Panel may apply this rule to a bidder who, together with any party acting in concert with it, has acquired less than 10% of our total ordinary shares in the 12-month period prior to the commencement of the offer period if the Irish Takeover Panel, taking into account the General Principles, considers it just and proper to do so.

An offer period will generally commence from the date of the first announcement of the offer or proposed offer.

Substantial Acquisition Rules

The Irish Takeover Rules also contain rules governing substantial acquisitions of shares which restrict the speed at which a person may increase his or her holding of shares and rights over shares to an aggregate of between 15% and 30% of our voting rights. Except in certain circumstances, an acquisition or series of acquisitions of shares or rights over shares representing 10% or more of our voting rights is prohibited if such acquisition(s), when aggregated with shares or rights already held, would result in the acquirer holding 15% or more but less than 30% of our voting rights and such acquisitions are made within a period of seven days. These rules also require accelerated disclosure of acquisitions of shares or rights over shares relating to such holdings.

Anti-Takeover Provisions

Shareholder Rights Plan

Our Articles of Association expressly authorize our board of directors to adopt a shareholder rights plan, subject to applicable law.

Frustrating Action

Under the Irish Takeover Rules, our board of directors is not permitted to take any action which might frustrate an offer for our shares once our board of directors has received an approach which may lead to an offer or has reason to believe an offer is imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of shares, options or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any time during which the board of directors has reason to believe an offer is imminent. Exceptions to this prohibition are available where:

- the action is approved by our shareholders at a general meeting; or
- the Irish Takeover Panel has given its consent, where:
    - it is satisfied the action would not constitute frustrating action;
    - our shareholders that hold 50% of the voting rights state in writing that they approve the proposed action and would vote in favor of it at a general meeting;
    - the action is taken in accordance with a contract entered into prior to the announcement of the offer; or
    - the decision to take such action was made before the announcement of the offer and either has been at least partially implemented or is in the ordinary course of business.

Business Combinations with Interested Shareholders

Our Articles of Association provide that, subject to certain exceptions, we may not engage in certain business combinations with any person that acquires beneficial ownership of 15% or more of our outstanding voting shares for a period of three years following the date on which the person became a 15% shareholder unless: (i) prior to the date on which the person becomes a 15% shareholder, a committee of our disinterested directors approved the business combination; and (ii) in certain circumstances, the business combination is authorized by a special resolution of disinterested shareholders.

Further Provisions

Certain other provisions of Irish law or our Constitution may be considered to have anti-takeover effects, including advance notice requirements for director nominations and other shareholder proposals, as well as those described under the headings "—Capital Structure—Authorized Share Capital" (regarding issuance of preferred shares), "—Pre-emption Rights, Share Warrants and Share Options," "—Disclosure of Interests in Shares," "—Appointment of Directors," and "—Removal of Directors."

Insider Dealing

The Irish Takeover Rules also provide that no person, other than the bidder, who is privy to confidential price-sensitive information concerning an offer made in respect of the acquisition of a company (or a class of its securities) or a contemplated offer shall deal in relevant securities of the target during the period from the time at which such person first has reason to suppose that such an offer, or an approach with a view to such an offer being made, is contemplated to the time of (i) the announcement of such offer or approach or (ii) the termination of discussions relating to such offer, whichever is earlier.

Corporate Governance

Our Articles of Association allocate authority over the day-to-day management of the Company to the board of directors. Our board of directors may then delegate management of the Company to committees of the board or such other persons as it thinks fit. Regardless of any delegation, the board of directors will remain responsible, as a matter of Irish law, for the proper management of the affairs of our Company. The board of directors may create new committees or change the responsibilities of existing committees from time to time. Committees may meet and adjourn as they determine proper. Unless otherwise determined by the board of directors, the quorum necessary for the transaction of business at any committee meeting shall be a majority of the members of the committee.

Appointment of Directors

The Irish Companies Act provides for a minimum of two directors. Our Articles of Association provide that the number of directors will be not less than two and not more than 13. The authorized number of directors within the prescribed range will be determined solely by our board of directors and does not require approval or ratification by the shareholders in a general meeting. Our directors will be elected by way of an ordinary resolution at a general meeting save that directors in contested elections will be elected by a plurality of the votes of the shares present in person or represented by proxy at the relevant general meeting and entitled to vote on the election of directors. If the number of the directors is reduced below the fixed minimum number, the remaining director or directors may appoint an additional director or additional directors to make up such minimum or may convene a general meeting for the purpose of making such appointment. Casual vacancies may be filled by the board of directors.

Our Articles of Association provide that our board of directors is divided into three classes serving staggered three-year terms. Shareholders do not have cumulative voting rights. Accordingly, the holder of a majority of the voting rights attaching to our ordinary shares will, as a practical matter, be entitled to control the election of all directors. At each annual general meeting, directors will be elected for a full term of three years to succeed those directors of the relevant class whose terms are expiring.

Under our Articles of Association, our board of directors has the authority to appoint directors to the board either to fill a vacancy or as an additional director. A vacancy on the board of directors created by the removal of a director may be filled by an ordinary resolution of the shareholders at the meeting at which such director is removed and, in the absence of such election or appointment, the remaining directors may fill the vacancy. The board of directors may fill a vacancy by an affirmative vote of a majority of the directors constituting a quorum. If there is an insufficient number of directors to constitute a quorum, the board may nonetheless act to fill such vacancies or call a general meeting of the shareholders. Under our Articles of Association, if the board fills a vacancy, the director will hold this position as a director for a term that will coincide with the remaining term of the relevant class of director. If there is an appointment to fill a casual vacancy or an addition to the board, the total number of directors shall not at any time exceed the number of directors from time to time fixed by the board in accordance with our Articles of Association.

Removal of Directors

The Irish Companies Act provides that, notwithstanding anything contained in the Articles of Association of a company or in any agreement between that company and a director, the shareholders may, by an ordinary resolution, remove a director from office before the expiration of his or her term, provided that notice of the intention to move any such resolution be given by the shareholders to the company not less than 28 days before the meeting at which the director is to be removed, and the director will be entitled to be heard at such meeting. The power of removal is without prejudice to any claim for damages for breach of contract (e.g., employment agreement) that the director may have against us in respect of his or her removal.

Director Interested Transactions

Under the Irish Companies Act and our Articles of Association, a director who has an interest in a proposal, arrangement or contract is required to declare the nature of his or her interest at the first opportunity either (i) at a meeting of the board at which such proposal, arrangement or contract is first considered (provided such director knows this interest then exists, or in any other case, at the first meeting of the board after learning that he or she is or has become so interested) or (ii) by providing a general notice to the directors declaring that he or she is to be regarded as interested in any proposal, arrangement or contract with a particular person, and after giving such

general notice will not be required to give special notice relating to any particular transaction. Provided the interested director makes such required disclosure, he or she shall be counted in determining the presence of a quorum at a meeting regarding the relevant proposal, arrangement or contract and will be permitted to vote on such proposal, arrangement or contract.

Pursuant to our Articles of Association, it is within the directors' sole discretion to determine their compensation.

Borrowing

Pursuant to our Articles of Association, among the directors' powers are the right to borrow money and to mortgage or charge the Company's undertaking, property and uncalled capital or any part thereof and to issue debentures, debenture stock, mortgages, bonds or such other securities whether outright or as security for any debt, liability or obligation of the Company or of any third party.

Duration; Dissolution; Rights upon Liquidation

Our duration will be unlimited. We may be dissolved and wound up at any time by way of a shareholders' voluntary winding up or a creditors' winding up. In the case of a shareholders' voluntary winding-up, a special resolution of shareholders is required. We may also be dissolved by way of court order on the application of a creditor, or by the Companies Registration Office as an enforcement measure where we have failed to file certain returns. We may also be dissolved by the Director of Corporate Enforcement in Ireland where the affairs of the Company have been investigated by an inspector and it appears from the report or any information obtained by the Director of Corporate Enforcement that we should be wound up.

The rights of the shareholders to a return of our assets on dissolution or winding up, following the settlement of all claims of creditors, are prescribed in our Articles of Association or the terms of any shares issued by the directors from time to time. The holders of preferred shares in particular may have the right to priority in a dissolution or winding up. If the Articles of Association and terms of issue of the shares of the Company contain no specific provisions in respect of a dissolution or winding up then, subject to the shareholder priorities and the rights of any creditors, the assets will be distributed to shareholders in proportion to the paid-up nominal value of the shares held. Our Articles of Association provide that our ordinary shareholders may be entitled to participate in a winding up, and the method by which the property will be divided shall be determined by the liquidator, subject to a special resolution of the shareholders, but such rights of ordinary shareholders to participate may be subject to the rights of any preferred shareholders to participate under the terms of any series or class of preferred shares.

Share Certificates

Pursuant to the Irish Companies Act, a shareholder is entitled to be issued a share certificate on request and subject to payment of a nominal fee.

Stock Exchange Listing

Our ordinary shares are listed on the Nasdaq Capital Market under the symbol "ITRM." Our ordinary shares are not listed on the Euronext Dublin.

No Sinking Fund

Our shares have no sinking fund provisions.

Transfer and Registration of Shares

Our transfer agent is Computershare Trust Company, N.A. The transfer agent maintains our share register, and registration in the share register will be determinative of membership in us. A shareholder of ours who only holds shares beneficially will not be the holder of record of such shares. Instead, the depository or other nominee will be the holder of record of those shares. Accordingly, a transfer of shares from a person who holds such shares beneficially to a person who also holds such shares beneficially through a depository or other nominee will not be

registered in our official share register, as the depository or other nominee will remain the record holder of any such shares.

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

Any transfer of our shares that is subject to Irish stamp duty will not be registered in the name of the buyer unless an instrument of transfer is duly stamped and provided to our transfer agent. Our Articles of Association allow us, in our absolute discretion, to create an instrument of transfer and pay (or procure the payment of) any stamp duty, which is the legal obligation of a transferee. In the event of any such payment, we are (on behalf of ourselves or our affiliates) entitled to (i) seek reimbursement from the transferee or transferor (at its discretion), (ii) set-off the amount of the stamp duty against future dividends payable to the transferee or transferor (at its discretion) and (iii) have a lien against the shares on which it has paid stamp duty. Parties to a share transfer may assume that any stamp duty arising in respect of a transaction in our shares has been paid unless one or both of such parties is otherwise notified by us.

Our Articles of Association delegate to our secretary (or such other person as may be nominated by the secretary for this purpose) the authority to execute an instrument of transfer on behalf of a transferring party.

Our Articles of Association grant our board of directors general discretion to decline to register an instrument of transfer unless the transfer is in respect of one class of shares only, the instrument of transfer is accompanied by the certificate of shares to which it relates (if any) and such other evidence as the directors may reasonably require to show the right of the transferor to make the transfer, the instrument of transfer is in favor of not more than four transferees and it is lodged at our registered office or such other place as our directors or secretary may appoint.

The directors may suspend registration of transfers from time to time, not exceeding 30 days in aggregate each year, as our board of directors may from time to time determine (except as may be required by law).

Exhibit 10.28

SECURITIES PURCHASE AGREEMENT

This Securities Purchase Agreement (this "Agreement") is dated as of February 9, 2021, between Iterum Therapeutics plc, an Irish incorporated public limited company (the "Company"), and each purchaser identified on the signature pages hereto (each, including its successors and assigns, a "Purchaser" and collectively the "Purchasers").

WHEREAS, subject to the terms and conditions set forth in this Agreement and pursuant to an effective registration statement under the Securities Act of 1933, as amended (the "Securities Act"), the Company desires to issue and sell to each Purchaser, and each Purchaser, severally and not jointly, desires to purchase from the Company, securities of the Company as more fully described in this Agreement.

NOW, THEREFORE, IN CONSIDERATION of the mutual covenants contained in this Agreement, and for other good and valuable consideration the receipt and adequacy of which are hereby acknowledged, the Company and each Purchaser agree as follows:

ARTICLE I.
DEFINITIONS

1.1 Definitions. In addition to the terms defined elsewhere in this Agreement, for all purposes of this Agreement, the following terms have the meanings set forth in this Section 1.1:

"Acquiring Person" shall have the meaning ascribed to such term in Section 4.5.

"Action" shall have the meaning ascribed to such term in Section 3.1(j).

"Affiliate" means any Person that, directly or indirectly through one or more intermediaries, controls or is controlled by or is under common control with a Person as such terms are used in and construed under Rule 405 under the Securities Act.

"Board of Directors" means the board of directors of the Company.

"Business Day" means any day other than Saturday, Sunday or other day on which commercial banks in The City of New York are authorized or required by law to remain closed; provided, however, for clarification, commercial banks shall not be deemed to be authorized or required by law to remain closed due to "stay at home", "shelter-in-place", "non-essential employee" or any other similar orders or restrictions or the closure of any physical branch locations at the direction of any governmental authority so long as the electronic funds transfer systems (including for wire transfers) of commercial banks in The City of New York generally are open for use by customers on such day.

"Closing" means the closing of the purchase and sale of the Securities pursuant to Section 2.1.

"Closing Date" means the Trading Day on which all of the Transaction Documents have been executed and delivered by the applicable parties thereto, and all conditions precedent to (i) the Purchasers' obligations to pay the Subscription Amount and (ii) the Company's obligations to deliver the Securities, in each case, have been satisfied or waived, but in no event later than the second (2nd) Trading Day following the date hereof, unless otherwise agreed in writing by the Company and a Purchaser with respect to the payment of such Purchaser's Subscription Amount and/or the delivery of such Purchaser's Shares.

"Commission" means the United States Securities and Exchange Commission.

"Company Irish Counsel " means A&L Goodbody, with offices located at International Financial Services Centre, North Wall Quay, Dublin 1, D01H104, Ireland.

"Company U.S. Counsel" means Wilmer Cutler Pickering Hale and Dorr LLP, with offices located at 7 World Trade Center, 250 Greenwich Street, New York, NY 10007.

"Disclosure Schedules" means the Disclosure Schedules of the Company delivered concurrently herewith.

"Disclosure Time" means, (i) if this Agreement is signed on a day that is not a Trading Day or after 9:00 a.m. (New York City time) and before midnight (New York City time) on any Trading Day, 9:01 a.m. (New York City time) on the Trading Day immediately following the date hereof, unless otherwise instructed as to an earlier time by the Placement Agent and the Company, and (ii) if this Agreement is signed between midnight (New York City time) and 9:00 a.m. (New York City time) on any Trading Day, no later than 9:01 a.m. (New York City time) on the date hereof, unless otherwise instructed as to an earlier time by the Placement Agent and the Company.

"Evaluation Date" shall have the meaning ascribed to such term in Section 3.1(s).

"Exchange Act" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

"Exempt Issuance" means the issuance of (a) Ordinary Shares or options or restricted share units or other equity awards to employees, officers or directors of the Company pursuant to any share or option plan duly adopted for such purpose, by a majority of the non-employee members of the Board of Directors or a majority of the members of a committee of non-employee directors established for such purpose for services rendered to the Company, (b) warrants issued to the Placement Agent in connection with the transactions pursuant to this Agreement and any securities upon exercise of warrants to the Placement Agent and/or securities upon the exercise or exchange of or conversion of any Securities issued hereunder and/or other securities exercisable or exchangeable for or convertible into Ordinary Shares issued and outstanding on the date of this Agreement, provided that such securities have not been amended since the date of this Agreement to increase the number of such securities or to

decrease the exercise price, exchange price or conversion price of such securities (other than in accordance with their terms) or to extend the term of such securities, (c) securities issued pursuant to Section 6 of the Investor Rights Agreement, dated as of January 21, 2020, by and among Iterum Therapeutics Bermuda Limited, the Company, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and the Purchasers (collectively, the "Parties") named in that certain Securities Purchase Agreement by and among the Parties dated as of January 16, 2020 (the "Investor Rights Agreement"), (d) securities issued pursuant to acquisitions or strategic transactions approved by a majority of the disinterested directors of the Company, provided that such securities are issued as "restricted securities" (as defined in Rule 144) and carry no registration rights that require or permit the filing of any registration statement in connection therewith during the prohibition period in Section 4.10 herein, and provided that any such issuance shall only be to a Person (or to the equityholders of a Person) which is, itself or through its subsidiaries, an operating company or an owner of an asset in a business synergistic with the business of the Company and shall provide to the Company additional benefits in addition to the investment of funds, but shall not include a transaction in which the Company is issuing securities primarily for the purpose of raising capital or to an entity whose primary business is investing in securities, and (e) any option shares issued to the Placement Agent in connection with an exercise of the over-allotment option pursuant to Section 2.2 of that certain Amended and Restated Underwriting Agreement dated February 3, 2021 by and between the Company and the Placement Agent (as the representative of the underwriters).

"FCPA" means the Foreign Corrupt Practices Act of 1977, as amended.

"FDA" shall have the meaning ascribed to such term in Section 3.1(hh).

"FDCA" shall have the meaning ascribed to such term in Section 3.1(hh).

"GAAP" shall have the meaning ascribed to such term in Section 3.1(h).

"Indebtedness" shall have the meaning ascribed to such term in Section 3.1(aa).

"Intellectual Property Rights" shall have the meaning ascribed to such term in Section 3.1(p).

"Liens" means a lien, charge, pledge, security interest, encumbrance, right of first refusal, preemptive right or other restriction.

"Lock-Up Agreement" means the Lock-Up Agreement, dated as of the date hereof, by each of the Company's officers and directors, in the form of Exhibit A attached hereto.

"Material Adverse Effect" shall have the meaning assigned to such term in Section 3.1(b).

"Material Permits" shall have the meaning ascribed to such term in Section 3.1(n).

"Ordinary Share" means the ordinary shares of the Company, nominal value $0.01 per share, and any other class of securities into which such securities may hereafter be reclassified or changed.

"Ordinary Share Equivalents" means any securities of the Company or the Subsidiaries which would entitle the holder thereof to acquire at any time Ordinary Shares, including, without limitation, any debt, preferred share, right, option, warrant or other instrument that is at any time convertible into or exercisable or exchangeable for, or otherwise entitles the holder thereof to receive, Ordinary Shares.

"Per Share Purchase Price" equals $2.00, subject to adjustment for reverse and forward share splits, share dividends, share combinations and other similar transactions of the Ordinary Shares that occur after the date of this Agreement and prior to the Closing Date.

"Person" means an individual or corporation, partnership, trust, incorporated or unincorporated association, joint venture, limited liability company, joint share company, government (or an agency or subdivision thereof) or other entity of any kind.

"Pharmaceutical Product" shall have the meaning ascribed to such term in Section 3.1(hh).

"Placement Agent" means H.C. Wainwright & Co., LLC.

"Proceeding" means an action, claim, suit, investigation or proceeding (including, without limitation, an informal investigation or partial proceeding, such as a deposition), whether commenced or threatened.

"Prospectus" means the final base prospectus filed for the Registration Statement, including the documents incorporated by reference therein.

"Prospectus Supplement" means the supplement to the Prospectus complying with Rule 424(b) of the Securities Act that is filed with the Commission and delivered by the Company to each Purchaser at the closing, including the documents incorporated by reference therein.

"Purchaser Party" shall have the meaning ascribed to such term in Section 4.7.

"Registration Statement" means the effective registration statement on Form S-3 with Commission file No. 333-232569 which registers the sale of the Shares to the Purchasers, including the documents incorporated by reference therein and the information deemed to be a part thereof pursuant to Rule 430B under the Securities Act.

"Required Approvals" shall have the meaning ascribed to such term in Section 3.1(e).

"Rule 144" means Rule 144 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended or interpreted from time to time, or any

similar rule or regulation hereafter adopted by the Commission having substantially the same purpose and effect as such Rule.

"Rule 424" means Rule 424 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended or interpreted from time to time, or any similar rule or regulation hereafter adopted by the Commission having substantially the same purpose and effect as such Rule.

"Rule 462(b) Registration Statement" means any registration statement prepared by the Company registering additional Securities, which was filed with the Commission on or prior to the date hereof and became automatically effective pursuant to Rule 462(b) promulgated by the Commission pursuant to the Securities Act.

"SEC Reports" shall have the meaning ascribed to such term in Section 3.1(h).

"Securities" means the Shares.

"Securities Act" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"Shares" means the Ordinary Shares issued or issuable to each Purchaser pursuant to this Agreement.

"Short Sales" means all "short sales" as defined in Rule 200 of Regulation SHO under the Exchange Act (but shall not be deemed to include locating and/or borrowing Ordinary Shares).

"Subscription Amount" means, as to each Purchaser, the aggregate amount to be paid for Shares purchased hereunder as specified below such Purchaser's name on the signature page of this Agreement and next to the heading "Subscription Amount," in United States dollars and in immediately available funds.

"Subsidiary" means any subsidiary of the Company as set forth in the SEC Reports and shall, where applicable, also include any direct or indirect subsidiary of the Company formed or acquired after the date hereof.

"Trading Day" means a day on which the principal Trading Market is open for trading.

"Trading Market" means any of the following markets or exchanges on which the Ordinary Shares are listed or quoted for trading on the date in question: the NYSE American, the Nasdaq Capital Market, the Nasdaq Global Market, the Nasdaq Global Select Market or the New York Stock Exchange (or any successors to any of the foregoing).

"Transaction Documents" means this Agreement, all exhibits and schedules thereto and hereto and any other documents or agreements executed with the Purchasers in connection with the transactions contemplated hereunder.

"Transfer Agent" means Computershare Trust Company, N.A., the current transfer agent of the Company, and any successor transfer agent of the Company.

"Variable Rate Transaction" shall have the meaning ascribed to such term in Section 4.10(b).

ARTICLE II.
PURCHASE AND SALE

2.1 Closing. On the Closing Date, upon the terms and subject to the conditions set forth herein, substantially concurrent with the execution and delivery of this Agreement by the parties hereto, the Company agrees to issue and sell, and the Purchasers, severally and not jointly, agree to purchase, up to an aggregate of $35,000,000 of Shares. Each Purchaser's Subscription Amount as set forth on the signature page hereto executed by such Purchaser shall be made available for "Delivery Versus Payment" settlement with the Company or its designee. The Company shall deliver to each Purchaser its respective Shares as determined pursuant to Section 2.2(a) and the Company and each Purchaser shall deliver the other items set forth in Section 2.2 deliverable at the Closing. Upon satisfaction of the covenants and conditions set forth in Sections 2.2 and 2.3, the Closing shall occur at the offices of the Placement Agent or such other location as the parties shall mutually agree. Unless otherwise directed by the Placement Agent, settlement of the Shares shall occur via "Delivery Versus Payment" ("DVP") (i.e., on the Closing Date, the Company shall issue the Shares registered in the Purchasers' names and addresses and released by the Transfer Agent directly to the account(s) at the Placement Agent identified by each Purchaser; upon receipt of such Shares, the Placement Agent shall promptly electronically deliver such Shares to the applicable Purchaser, and payment therefor shall be made by the Placement Agent (or its clearing firm) by wire transfer to the Company). Notwithstanding anything herein to the contrary, if at any time on or after the time of execution of this Agreement by the Company and an applicable Purchaser, through, and including the time immediately prior to the Closing (the "Pre-Settlement Period"), if such Purchaser sells to any Person all, or any portion, of any Ordinary Shares to be issued hereunder to such Purchaser at the Closing (collectively, the "Pre-Settlement Shares"), such Purchaser shall, automatically hereunder (without any additional required actions by such Purchaser or the Company), be deemed to be unconditionally bound to purchase, and the Company shall be deemed unconditionally bound to sell, such Pre-Settlement Shares to such Purchaser at the Closing; provided, that the Company shall not be required to deliver any Pre-Settlement Shares to such Purchaser prior to the Company's receipt of the Subscription Amount for such Pre-Settlement Shares hereunder; provided, further, that the Company hereby acknowledges and agrees that the forgoing shall not constitute a representation or covenant by such Purchaser as to whether or not such Purchaser will elect to sell any Pre-Settlement Shares during the Pre-Settlement Period. The decision to sell any Ordinary Shares will be made in the sole discretion of such Purchaser from time to time, including during the Pre-Settlement Period.

2.2 Deliveries.

(a) On or prior to the Closing Date (except as indicated below), the Company shall deliver or cause to be delivered to each Purchaser the following:

(i) this Agreement duly executed by the Company;

(ii) a legal opinion of Company U.S. Counsel, in substantially the form set forth on Exhibit B hereto;

(iii) a legal opinion of Company Irish Counsel, in substantially the form set forth on Exhibit C hereto;

(iv) the Company shall have provided each Purchaser with the Company's wire instructions, on Company letterhead and executed by the Chief Executive Officer or Chief Financial Officer;

(v) subject to the penultimate sentence of Section 2.1, a copy of the irrevocable instructions to the Transfer Agent instructing the Transfer Agent to deliver on an expedited basis via The Depository Trust Company Deposit or Withdrawal at Custodian system ("DWAC") Shares equal to the portion of such Purchaser's Subscription Amount applicable to the Shares divided by the Per Share Purchase Price (rounded down to the nearest whole Share), registered in the name of such Purchaser;

(vi) duly execued Lock-Up Agreements; and

(vii) the Prospectus and the Prospectus Supplement (which may be delivered in accordance with Rule 172 under the Securities Act).

(b) On or prior to the Closing Date, each Purchaser shall deliver or cause to be delivered to the Company the following:

(i) this Agreement duly executed by such Purchaser; and

(ii) such Purchaser's Subscription Amount, which shall be made available for "Delivery Versus Payment" settlement with the Company or its designee.

2.3 Closing Conditions.

(a) The obligations of the Company hereunder in connection with the Closing are subject to the following conditions being met:

(i) the accuracy in all material respects (or, to the extent representations or warranties are qualified by materiality or Material Adverse Effect, in all respects) when made and on the Closing Date of the representations and warranties of the Purchasers contained herein (unless as of a specific date therein in which case they shall be accurate as of such date);

(ii) all obligations, covenants and agreements of each Purchaser required to be performed at or prior to the Closing Date shall have been performed; and

(iii) the delivery by each Purchaser of the items set forth in Section 2.2(b) of this Agreement.

(b) The respective obligations of the Purchasers hereunder in connection with the Closing are subject to the following conditions being met:

(i) the accuracy in all material respects (or, to the extent representations or warranties are qualified by materiality or Material Adverse Effect, in all respects) when made and on the Closing Date of the representations and warranties of the Company contained herein (unless as of a specific date therein in which case they shall be accurate as of such date);

(ii) all obligations, covenants and agreements of the Company required to be performed at or prior to the Closing Date shall have been performed;

(iii) the delivery by the Company of the items set forth in Section 2.2(a) of this Agreement;

(iv) there shall have been no Material Adverse Effect with respect to the Company since the date hereof; and

(v) from the date hereof to the Closing Date, trading in the Ordinary Shares shall not have been suspended by the Commission or the Company's principal Trading Market, and, at any time prior to the Closing Date, trading in securities generally on any nationally recognized securities exchange as reported by Bloomberg L.P. shall not have been suspended or limited, or minimum prices shall not have been established on securities whose trades are reported by such service, or on any Trading Market, nor shall a banking moratorium have been declared either by the United States or New York State authorities nor shall there have occurred any material outbreak or escalation of hostilities or other national or international calamity of such magnitude in its effect on, or any material adverse change in, any financial market which, in each case, in the reasonable judgment of such Purchaser, makes it impracticable or inadvisable to purchase the Securities at the Closing.

ARTICLE III.
REPRESENTATIONS AND WARRANTIES

3.1 Representations and Warranties of the Company. Except as set forth in the Disclosure Schedules, which Disclosure Schedules shall be deemed a part hereof and shall qualify any representation or otherwise made herein to the extent of the disclosure contained in the corresponding section of the Disclosure Schedules, the Company hereby makes the following representations and warranties to each Purchaser:

(a) Subsidiaries. All of the direct and indirect subsidiaries of the Company are set forth in the SEC Reports. Except as disclosed in the SEC Reports, (i) the Company owns, directly or indirectly, all of the share capital or other equity interests of each Subsidiary free and clear of any Liens and (ii) all of the issued and outstanding share

capital of each Subsidiary are validly issued and are fully paid and are not subject to any calls for additional payments (non-assessable) and free of preemptive and similar rights to subscribe for or purchase securities.

(b) Organization and Qualification. The Company and each of the Subsidiaries is an entity duly incorporated or otherwise organized, validly existing and in good standing under the laws of the jurisdiction of its incorporation or organization (or such equivalent concept to the extent such equivalent concept exists under the law of such jurisdiction), with the requisite power and authority to own and use its properties and assets and to carry on its business as currently conducted. Neither the Company nor any Subsidiary is in violation nor default of any of the provisions of its respective certificate or articles of incorporation, bylaws or other organizational or charter documents. Each of the Company and the Subsidiaries is duly qualified to conduct business and is in good standing (or such equivalent concept to the extent such equivalent concept exists under the law of such jurisdiction) as a foreign corporation or other entity in each jurisdiction in which the nature of the business conducted or property owned by it makes such qualification necessary, except where the failure to be so qualified or in good standing, as the case may be, would not have or reasonably be expected to result in: (i) a material adverse effect on the legality, validity or enforceability of any Transaction Document, (ii) a material adverse effect on the results of operations, assets, business, prospects or condition (financial or otherwise) of the Company and the Subsidiaries, taken as a whole, or (iii) a material adverse effect on the Company's ability to perform its obligations under the Transaction Documents (any of (i), (ii) or (iii), a "Material Adverse Effect"), provided that changes in the trading price of the Ordinary Shares shall not, in and of itself, constitute a Material Adverse Effect, and no Proceeding has been instituted in any such jurisdiction revoking, limiting or curtailing or seeking to revoke, limit or curtail such power and authority or qualification.

(c) Authorization; Enforcement. The Company has the requisite corporate power and authority to enter into and to consummate the transactions contemplated by this Agreement and each of the other Transaction Documents and otherwise to carry out its obligations hereunder and thereunder. The execution and delivery of this Agreement and each of the other Transaction Documents by the Company and the consummation by it of the transactions contemplated hereby and thereby have been duly authorized by all necessary action on the part of the Company and no further action is required by the Company, the Board of Directors or the Company's shareholders in connection herewith or therewith other than in connection with the Required Approvals. This Agreement and each other Transaction Document to which it is a party has been (or upon delivery will have been) duly executed by the Company and, when delivered in accordance with the terms hereof and thereof, will constitute the valid and binding obligation of the Company enforceable against the Company in accordance with its terms, except (i) as limited by general equitable principles and applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting enforcement of creditors' rights generally, (ii) as limited by laws relating to the availability of specific performance, injunctive relief or other equitable remedies and (iii) insofar as indemnification and contribution provisions may be limited by applicable law.

(d) No Conflicts. Except as disclosed in the Prospectus or the Prospectus Supplement, the execution, delivery and performance by the Company of this Agreement and the other Transaction Documents to which it is a party, the issuance and sale of the Securities and the consummation by it of the transactions contemplated hereby and thereby do not and will not (i) conflict with or violate any provision of the Company's or any Subsidiary's certificate or articles of association or incorporation, bylaws or other organizational or charter documents, or (ii) conflict with, or constitute a default (or an event that with notice or lapse of time or both would become a default) under, result in the creation of any Lien upon any of the properties or assets of the Company or any Subsidiary, or give to others any rights of termination, amendment, anti-dilution or similar adjustments, acceleration or cancellation (with or without notice, lapse of time or both) of, any agreement, credit facility, debt or other instrument (evidencing a Company or Subsidiary debt or otherwise) to which the Company or any Subsidiary is a party or by which any property or asset of the Company or any Subsidiary is bound or affected, or (iii) subject to the Required Approvals, conflict with or result in a violation of any law, rule, regulation, order, judgment, injunction, decree or other restriction of any court or governmental authority to which the Company or a Subsidiary is subject (including federal and state securities laws and regulations), or by which any property or asset of the Company or a Subsidiary is bound or affected; except in the case of each of clauses (ii) and (iii), such as would not have or reasonably be expected to result in a Material Adverse Effect.

(e) Filings, Consents and Approvals. The Company is not required to obtain any consent, waiver, authorization or order of, give any notice to, or make any filing or registration with, any court or other federal, state, local or other governmental authority or other Person in connection with the execution, delivery and performance by the Company of the Transaction Documents, other than: (i) the filings required pursuant to Section 4.3 of this Agreement, (ii) the filing with the Commission of the Prospectus Supplement, (iii) application(s) to each applicable Trading Market for the listing of the Shares for trading thereon in the time and manner required thereby, and (iv) such filings as are required to be made under applicable state securities laws, or the laws of Ireland, or the rules of the Financial Industry Regulatory Authority, Inc. ("FINRA") (collectively, the "Required Approvals").

(f) Issuance of the Securities; Registration. The Securities are duly authorized and, when issued and paid for in accordance with the applicable Transaction Documents, will be duly and validly issued, fully paid and not subject to any calls for additional capital (nonassessable), free and clear of all Liens imposed by the Company. The Company will reserve from its duly authorized share capital the maximum number of Ordinary Shares issuable pursuant to this Agreement. The Company has prepared and filed the Registration Statement in conformity with the requirements of the Securities Act, which originally became effective on July 16, 2019 (the "Effective Date"), including the Prospectus, and such amendments and supplements thereto as may have been required to the date of this Agreement. The Registration Statement is effective under the Securities Act and no stop order preventing or suspending the effectiveness of the Registration Statement or suspending or preventing the use of the Prospectus or the Prospectus Supplement has been issued by the Commission and no proceedings for that

purpose have been instituted or, to the knowledge of the Company, are threatened by the Commission. The Company, if required by the rules and regulations of the Commission, shall file the Prospectus Supplement with the Commission pursuant to Rule 424(b). At the time the Registration Statement and any amendments thereto became effective, at the date of this Agreement and at the Closing Date, the Registration Statement and any amendments thereto conformed and will conform in all material respects to the requirements of the Securities Act and did not and will not contain any untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading; and the Prospectus Supplement and any amendments or supplements thereto, at the time the Prospectus Supplement, or any amendment or supplement thereto was issued and at the Closing Date, conformed and will conform in all material respects to the requirements of the Securities Act and did not and will not contain an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The Company was at the time of the filing of the Registration Statement eligible to use Form S-3. The Company is eligible to use Form S-3 under the Securities Act and it meets the transaction requirements as set forth in General Instruction I.B.1 of Form S-3.

(g) Capitalization. The authorized capitalization of the Company is set forth in the SEC Reports. Except as disclosed in the Prospectus or the Prospectus Supplement or in the SEC Reports, the Company has not issued any share capital since its most recently filed periodic report under the Exchange Act, other than pursuant to the exercise of share options or the vesting of restricted share awards under the Company's equity plans by employees, directors or other service providers, the issuance of Ordinary Shares to employees, directors or other service providers pursuant to the Company's equity plans and pursuant to the conversion and/or exercise of Ordinary Share Equivalents outstanding as of the date of or described in the most recently filed periodic report under the Exchange Act. Except as disclosed in Schedule 3.1(g) or been waived, no Person has any right of first refusal, preemptive right, right of participation, or any similar right to participate in the transactions contemplated by the Transaction Documents. Except for the Securities to be issued and sold hereunder or as disclosed in the SEC Reports or Schedule 3.1(g), there are no outstanding options, warrants, scrip rights to subscribe to, calls or commitments of any character whatsoever relating to, or securities, rights or obligations convertible into or exercisable or exchangeable for, or giving any Person any right to subscribe for or acquire, any Ordinary Shares or the share capital of any Subsidiary, or contracts, commitments, understandings or arrangements by which the Company or any Subsidiary is or may become bound to issue additional Ordinary Shares or Ordinary Share Equivalents or share capital of any Subsidiary. Except as disclosed in Schedule 3.1(g), the issuance and sale of the Securities will not obligate the Company or any Subsidiary to issue Ordinary Shares or other securities to any Person (other than the Purchasers). Except as disclosed in the SEC Reports and the Prospectus Supplement, there are no outstanding securities or instruments of the Company or any Subsidiary with any provision that adjusts the exercise, conversion, exchange or reset price of such security or instrument upon an issuance of securities by the Company or any Subsidiary. Except as disclosed in the SEC Reports, there are no outstanding securities or instruments of the Company or any Subsidiary that contain any redemption or similar provisions, and

there are no contracts, commitments, understandings or arrangements by which the Company or any Subsidiary is or may become bound to redeem a security of the Company or such Subsidiary. Except as disclosed in the SEC Reports, the Company does not have any share appreciation rights or "phantom share" plans or agreements or any similar plan or agreement other than as disclosed in the SEC Reports. All of the outstanding share capital of the Company is duly authorized, validly issued, fully paid and not subject to any calls for additional payments (nonassessable), has been issued in compliance with all federal and state securities laws, and none of such outstanding shares was issued in violation of any preemptive rights or similar rights to subscribe for or purchase securities. No further approval or authorization of any shareholder, the Board of Directors or others is required for the issuance and sale of the Securities. Except as disclosed in the SEC Reports, there are no shareholders agreements, voting agreements or other similar agreements with respect to the Company's share capital to which the Company is a party or, to the knowledge of the Company, between or among any of the Company's shareholders.

(h) SEC Reports; Financial Statements. The Company has filed all reports, schedules, forms, statements and other documents required to be filed by the Company under the Securities Act and the Exchange Act, including pursuant to Section 13(a) or 15(d) thereof, for the two years preceding the date hereof (or such shorter period as the Company was required by law or regulation to file such material) (the foregoing materials, including the exhibits thereto and documents incorporated by reference therein, together with the Prospectus and the Prospectus Supplement, being collectively referred to herein as the "SEC Reports") on a timely basis or has received a valid extension of such time of filing and has filed any such SEC Reports prior to the expiration of any such extension. As of their respective dates, the SEC Reports complied in all material respects with the requirements of the Securities Act and the Exchange Act, as applicable, and none of the SEC Reports, when filed, contained any untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The Company has never been an issuer subject to Rule 144(i) under the Securities Act. The financial statements of the Company included in the SEC Reports comply in all material respects with applicable accounting requirements and the rules and regulations of the Commission with respect thereto as in effect at the time of filing. Such financial statements have been prepared in accordance with United States generally accepted accounting principles applied on a consistent basis during the periods involved ("GAAP"), except as may be otherwise specified in such financial statements or the notes thereto and except that unaudited financial statements may not contain all footnotes required by GAAP, and fairly present in all material respects the financial position of the Company and its consolidated Subsidiaries as of and for the dates thereof and the results of operations and cash flows for the periods then ended, subject, in the case of unaudited statements, to normal, immaterial, year-end audit adjustments.

(i) Material Changes; Undisclosed Events, Liabilities or Developments. Since the date of the most recent unaudited financial statements included within the SEC Reports, except as set forth in the SEC Reports, (i) there has been no event, occurrence or development that has had or that would reasonably be expected to result in a Material

Adverse Effect, (ii) the Company has not incurred any liabilities (contingent or otherwise) other than (A) payables and other accrued expenses incurred in the ordinary course of business consistent with past practice and (B) liabilities not required to be reflected in the Company's financial statements pursuant to GAAP or disclosed in filings made with the Commission, (iii) the Company has not altered its method of accounting, (iv) the Company has not declared or made any dividend or distribution of cash or other property to its shareholders or purchased, redeemed or made any agreements to purchase or redeem any of its share capital and (v) the Company has not issued any equity securities to any officer, director or Affiliate, except pursuant to existing Company equity plans. The Company does not have pending before the Commission any request for confidential treatment of information. Except for the issuance of the Securities contemplated by this Agreement or as set forth in the SEC Reports, no material event, liability, fact, circumstance, occurrence or development has occurred or exists or is reasonably expected to occur or exist with respect to the Company or its Subsidiaries or their respective businesses, prospects, properties, operations, assets or financial condition that would be required to be disclosed by the Company under applicable securities laws at the time this representation is made or deemed made that has not been publicly disclosed prior to the time of execution of this Agreement.

(j) Litigation . Except as disclosed in Schedule 3.1(j), there is no action, suit, inquiry, notice of violation, proceeding or investigation pending or, to the knowledge of the Company, threatened against or affecting the Company, any Subsidiary or any of their respective properties before or by any court, arbitrator, governmental or administrative agency or regulatory authority (federal, state, county, local or foreign) (collectively, an "Action") which (i) adversely affects or challenges the legality, validity or enforceability of any of the Transaction Documents or the Securities or (ii) would, if there were an unfavorable decision, have or reasonably be expected to result in a Material Adverse Effect. Except as disclosed in the SEC Reports, neither the Company nor any Subsidiary, nor any director or officer (in his or her capacity as such) thereof, is or has been the subject of any Action involving a claim of violation of or liability under federal or state securities laws or a claim of breach of fiduciary duty. There has not been, and to the knowledge of the Company, there is not pending or contemplated, any investigation by the Commission involving the Company or any current or former director or officer of the Company (in his or her capacity as such). The Commission has not issued any stop order or other order suspending the effectiveness of any registration statement filed by the Company or any Subsidiary under the Exchange Act or the Securities Act.

(k) Labor Relations . No labor dispute exists or, to the knowledge of the Company, is imminent with respect to any of the employees of the Company, which would reasonably be expected to result in a Material Adverse Effect. The Company and its Subsidiaries believe that their relationships with their employees are good. To the knowledge of the Company, no executive officer of the Company or any Subsidiary, is, or is now expected to be, in violation of any material term of any employment contract, confidentiality, disclosure or proprietary information agreement or non-competition agreement, or any other contract or agreement or any restrictive covenant in favor of any third party, and the continued employment of each such executive officer does not subject the Company or any of its Subsidiaries to any liability with respect to any of the

foregoing matters. The Company and its Subsidiaries are in compliance with all U.S. federal, state, local and foreign laws and regulations relating to employment and employment practices, terms and conditions of employment and wages and hours, except where the failure to be in compliance would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect.

(l) Compliance. Neither the Company nor any Subsidiary: (i) is in default under or in violation of (and no event has occurred that has not been waived that, with notice or lapse of time or both, would result in a default by the Company or any Subsidiary under), nor has the Company or any Subsidiary received notice of a claim that it is in default under or that it is in violation of, any indenture, loan or credit agreement or any other agreement or instrument to which it is a party or by which it or any of its properties is bound (whether or not such default or violation has been waived), (ii) is in violation of any judgment, decree or order of any court, arbitrator or other governmental authority or (iii) is or has been in violation of any statute, rule, ordinance or regulation of any governmental authority, including without limitation all foreign, federal, state and local laws relating to taxes, environmental protection, occupational health and safety, product quality and safety and employment and labor matters, except, in the case of each of clauses (i), (ii) and (iii) as disclosed in the SEC Reports or as would not have or reasonably be expected to result in a Material Adverse Effect.

(m) Environmental Laws. The Company and its Subsidiaries (i) are in compliance with all federal, state, local and foreign laws relating to pollution or protection of human health or the environment (including ambient air, surface water, groundwater, land surface or subsurface strata), including laws relating to emissions, discharges, releases or threatened releases of chemicals, pollutants, contaminants, or toxic or hazardous substances or wastes (collectively, "Hazardous Materials") into the environment, or otherwise relating to the manufacture, processing, distribution, use, treatment, storage, disposal, transport or handling of Hazardous Materials, as well as all authorizations, codes, decrees, demands, or demand letters, injunctions, judgments, licenses, notices or notice letters, orders, permits, plans or regulations, issued, entered, promulgated or approved thereunder ("Environmental Laws"); (ii) have received all permits licenses or other approvals required of them under applicable Environmental Laws to conduct their respective businesses; and (iii) are in compliance with all terms and conditions of any such permit, license or approval where in each of clause (i), (ii) and (iii), the failure to so comply would be reasonably expected to have, individually or in the aggregate, a Material Adverse Effect.

(n) Regulatory Permits. The Company and the Subsidiaries possess all certificates, authorizations and permits issued by the appropriate federal, state, local or foreign regulatory authorities necessary to conduct their respective businesses as described in the SEC Reports, except where the failure to possess such permits would not reasonably be expected to result in a Material Adverse Effect ("Material Permits"), and neither the Company nor any Subsidiary has received any notice of proceedings relating to the revocation or modification of any Material Permit.

(o) Title to Assets. Except as disclosed in the SEC Reports, the Company and the Subsidiaries have good and marketable title in fee simple to all real property owned by them and good and marketable title in all personal property owned by them that is material to the business of the Company and the Subsidiaries, in each case free and clear of all Liens, except for (i) Liens as do not materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company and the Subsidiaries, and (ii) Liens for the payment of federal, state or other taxes, for which appropriate reserves have been made therefor in accordance with GAAP, and the payment of which is neither delinquent nor subject to penalties. Any real property and facilities held under lease by the Company and the Subsidiaries are held by them under valid, subsisting and enforceable leases with which the Company and the Subsidiaries are in compliance in all material respects.

(p) Intellectual Property. To the knowledge of the Company, the Company and the Subsidiaries have, or have rights to use, all patents, patent applications, trademarks, trademark applications, service marks, trade names, trade secrets, inventions, copyrights, licenses and other intellectual property rights and similar rights necessary or required for use in connection with their respective businesses as described in the SEC Reports and which the failure to so have would have a Material Adverse Effect (collectively, the "Intellectual Property Rights"). None of, and neither the Company nor any Subsidiary has received a written notice that any of, the material Intellectual Property Rights has expired, terminated or been abandoned, or is expected to expire or terminate or be abandoned, within two (2) years from the date of this Agreement, other than in accordance with the terms of the Intellectual Property Rights. Neither the Company nor any Subsidiary has received, since the date of the most recent unaudited financial statements included within the SEC Reports, a written notice of a claim or otherwise has any knowledge that the Intellectual Property Rights violate or infringe upon the rights of any Person, except as would not have or reasonably be expected to not have a Material Adverse Effect. To the knowledge of the Company, all such Intellectual Property Rights are enforceable and there is no existing infringement by another Person of any of the Intellectual Property Rights, except as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect. The Company and its Subsidiaries have taken reasonable security measures to protect the secrecy, confidentiality and value of all of their intellectual properties, except where failure to do so would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect. The Company has no knowledge of any facts that would preclude it from having valid license rights or clear title to the Intellectual Property Rights, except as would not have or reasonably be expected to not have a Material Adverse Effect. The Company has no knowledge that it lacks or will be unable to obtain any rights or licenses to use all Intellectual Property Rights that are necessary to conduct its business, except as would not have or reasonably be expected to not have a Material Adverse Effect.

(q) Insurance. The Company and the Subsidiaries are insured by insurers of recognized financial responsibility against such losses and risks and in such amounts as are prudent and customary in the businesses in which the Company and the Subsidiaries are engaged, including, but not limited to, directors and officers insurance coverage. Neither the Company nor any Subsidiary has any reason to believe that it will not be able

to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business without a significant increase in cost.

(r) Transactions With Affiliates and Employees. Except as set forth in the SEC Reports, none of the officers or directors of the Company or any Subsidiary and, to the knowledge of the Company, none of the employees of the Company or any Subsidiary is presently a party to any transaction with the Company or any Subsidiary (other than for services as employees, officers and directors), including any contract, agreement or other arrangement providing for the furnishing of services to or by, providing for rental of real or personal property to or from, providing for the borrowing of money from or lending of money to or otherwise requiring payments to or from any officer, director or such employee or, to the knowledge of the Company, any entity in which any officer, director, or any such employee has a substantial interest or is an officer, director, trustee, shareholder, member or partner, in each case in excess of $120,000 other than for (i) payment of salary or consulting fees for services rendered, (ii) reimbursement for expenses incurred on behalf of the Company and (iii) other employee benefits, including share option agreements under any equity plan of the Company.

(s) Sarbanes-Oxley; Internal Accounting Controls. The Company and the Subsidiaries are in compliance in all material respects with any and all applicable requirements of the Sarbanes-Oxley Act of 2002 that are effective as of the date hereof, and any and all applicable rules and regulations promulgated by the Commission thereunder that are effective as of the date hereof and as of the Closing Date. The Company and the Subsidiaries maintain a system of internal accounting controls sufficient to provide reasonable assurance that: (i) transactions are executed in accordance with management's general or specific authorizations, (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain asset accountability, (iii) access to assets is permitted only in accordance with management's general or specific authorization, and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. The Company and the Subsidiaries have established disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the Company and the Subsidiaries and designed such disclosure controls and procedures to ensure that information required to be disclosed by the Company in the reports it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Commission's rules and forms. The Company's certifying officers have evaluated the effectiveness of the disclosure controls and procedures of the Company and the Subsidiaries as of the end of the period covered by the most recently filed periodic report under the Exchange Act (such date, the "Evaluation Date"). The Company presented in its most recently filed periodic report under the Exchange Act the conclusions of the certifying officers about the effectiveness of the disclosure controls and procedures based on their evaluations as of the Evaluation Date. Since the Evaluation Date, there have been no changes in the internal control over financial reporting (as such term is defined in the Exchange Act) of the Company and its Subsidiaries that have materially affected, or

are reasonably likely to materially affect, the internal control over financial reporting of the Company and its Subsidiaries.

(t) Certain Fees. Except as set forth in the Prospectus Supplement, no brokerage or finder's fees or commissions are or will be payable by the Company or any Subsidiary to any broker, financial advisor or consultant, finder, placement agent, investment banker, bank or other Person with respect to the transactions contemplated by the Transaction Documents. The Purchasers shall have no obligation with respect to any fees or with respect to any claims made by or on behalf of other Persons for fees of a type contemplated in this Section that may be due in connection with the transactions contemplated by the Transaction Documents.

(u) Investment Company. The Company is not, and immediately after receipt of payment for the Securities will not be, an "investment company" within the meaning of the Investment Company Act of 1940, as amended. The Company shall conduct its business in a manner so that it will not become an "investment company" subject to registration under the Investment Company Act of 1940, as amended.

(v) Registration Rights. Except as disclosed in the SEC Reports, no Person has any right to cause the Company or any Subsidiary to effect the registration under the Securities Act of any securities of the Company or any Subsidiary.

(w) Listing and Maintenance Requirements. The Ordinary Shares are registered pursuant to Section 12(b) or 12(g) of the Exchange Act, and the Company has taken no action designed to, or which to its knowledge is likely to have the effect of, terminating the registration of the Ordinary Shares under the Exchange Act nor has the Company received any notification that the Commission is contemplating terminating such registration. Except as disclosed in the SEC Reports, the Company has not, in the 12 months preceding the date hereof, received notice from any Trading Market on which the Ordinary Shares are or have been listed or quoted to the effect that the Company is not in compliance with the listing or maintenance requirements of any Trading Market on which the Ordinary Shares are listed or quoted. The Ordinary Shares are currently eligible for electronic transfer through the Depository Trust Company or another established clearing corporation and the Company is current in payment of the fees to the Depository Trust Company (or such other established clearing corporation) in connection with such electronic transfer.

(x) Application of Takeover Protections. The Company and the Board of Directors have taken all necessary action, if any, in order to render inapplicable any control share acquisition, business combination, poison pill (including any distribution under a rights agreement) or other similar anti-takeover provision under the Company's articles of association (or similar charter documents) or the laws of its jurisdiction of incorporation that is or would become applicable to the Purchasers as a result of the Purchasers and the Company fulfilling their obligations or exercising their rights under the Transaction Documents, including without limitation as a result of the Company's issuance of the Securities and the Purchasers' ownership of the Securities.

(y) Disclosure. Except with respect to the material terms and conditions of the transactions contemplated by the Transaction Documents, the Company confirms that neither it nor any other Person acting on its behalf has provided any of the Purchasers or their agents or counsel with any information that it believes constitutes or might constitute material, non-public information which is not otherwise disclosed in the Prospectus Supplement. The Company understands and confirms that the Purchasers will rely on the foregoing representation in effecting transactions in securities of the Company. All of the disclosure furnished by or on behalf of the Company to the Purchasers regarding the Company and its Subsidiaries, their respective businesses and the transactions contemplated hereby is true and correct in all material respects and does not contain any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements made therein, in the light of the circumstances under which they were made, not misleading (it being understood that such disclosure furnished by or on behalf of the Company to the Purchasers includes the SEC Reports). The Company acknowledges and agrees that no Purchaser makes or has made any representations or warranties with respect to the transactions contemplated hereby other than those specifically set forth in Section 3.2 hereof.

(z) No Integrated Offering . Assuming the accuracy of the Purchasers' representations and warranties set forth in Section 3.2, neither the Company nor any of its Subsidiaries nor, to the Company's knowledge, any of its controlled Affiliates, nor any Person acting on its or their behalf (other than the Placement Agent), has, directly or indirectly, made any offers or sales of any security or solicited any offers to buy any security, under circumstances that would cause this offering of the Securities to be integrated with prior offerings by the Company for purposes of any applicable shareholder approval provisions of any Trading Market on which any of the securities of the Company are listed or designated in a manner that would require shareholder approval for the issuance of the Securities.

(aa) Solvency. The Company has no current intention of filing for reorganization or liquidation under the bankruptcy or reorganization laws of any jurisdiction. The SEC Reports set forth as of the date hereof all outstanding secured and unsecured Indebtedness of the Company or any Subsidiary, or for which the Company or any Subsidiary has commitments. For the purposes of this Agreement, "Indebtedness " means (x) any liabilities for borrowed money or amounts owed in excess of $50,000 (other than trade accounts payable incurred in the ordinary course of business), (y) all guaranties, endorsements and other contingent obligations in respect of indebtedness of others, whether or not the same are or should be reflected in the Company's consolidated balance sheet (or the notes thereto), except guaranties by endorsement of negotiable instruments for deposit or collection or similar transactions in the ordinary course of business; and (z) the present value of any lease payments in excess of $50,000 due under leases required to be capitalized in accordance with GAAP. Neither the Company nor any Subsidiary is in default with respect to any Indebtedness.

(bb) Tax Status. Except for matters that would not, individually or in the aggregate, have or reasonably be expected to result in a Material Adverse Effect, the Company and its Subsidiaries each (i) has made or filed all United States federal, state

and local income and all foreign income and franchise tax returns, reports and declarations required by any jurisdiction to which it is subject, (ii) has paid all taxes and other governmental assessments and charges that are material in amount, shown or determined to be due on such returns, reports and declarations, except for such taxes, if any, as are being contested in good faith and as to which adequate reserves have been established by the Company and (iii) has set aside on its books provision reasonably adequate for the payment of all material taxes for periods subsequent to the periods to which such returns, reports or declarations apply. There are no unpaid taxes in any material amount claimed to be due by the taxing authority of any jurisdiction, and the officers of the Company or of any Subsidiary know of no basis for any such claim.

(cc) Foreign Corrupt Practices. Neither the Company nor any Subsidiary, nor to the knowledge of the Company or any Subsidiary, any agent or other person acting on behalf of the Company or any Subsidiary, has (i) directly or indirectly, used any funds for unlawful contributions, gifts, entertainment or other unlawful expenses related to foreign or domestic political activity, (ii) made any unlawful payment to foreign or domestic government officials or employees or to any foreign or domestic political parties or campaigns from corporate funds, (iii) failed to disclose fully any contribution made by the Company or any Subsidiary (or made by any person acting on its behalf of which the Company is aware) which is in violation of law, or (iv) violated in any material respect any provision of FCPA.

(dd) Accountants. The Company's independent registered public accounting firm is KPMG. To the knowledge and belief of the Company, such accounting firm (i) is a registered public accounting firm as required by the Exchange Act and (ii) shall express its opinion with respect to the financial statements to be included in the Company's Annual Report for the fiscal year ending December 31, 2020.

(ee) Acknowledgment Regarding Purchasers' Purchase of Securities. The Company acknowledges and agrees that each of the Purchasers is acting solely in the capacity of an arm's length purchaser with respect to the Transaction Documents and the transactions contemplated thereby. The Company further acknowledges that no Purchaser is acting as a financial advisor or fiduciary of the Company (or in any similar capacity) with respect to the Transaction Documents and the transactions contemplated thereby and any advice given by any Purchaser or any of their respective representatives or agents in connection with the Transaction Documents and the transactions contemplated thereby is merely incidental to the Purchasers' purchase of the Securities. The Company further represents to each Purchaser that the Company's decision to enter into this Agreement and the other Transaction Documents has been based solely on the independent evaluation of the transactions contemplated hereby by the Company and its representatives.

(ff) Acknowledgment Regarding Purchaser's Trading Activity. Anything in this Agreement or elsewhere herein to the contrary notwithstanding (except for Sections 3.2(f) and 4.12 hereof), it is understood and acknowledged by the Company that: (i) none of the Purchasers has been asked by the Company to agree, nor has any Purchaser agreed, to desist from purchasing or selling, long and/or short, securities of the Company, or

"derivative" securities based on securities issued by the Company or to hold the Securities for any specified term; (ii) past or future open market or other transactions by any Purchaser, specifically including, without limitation, Short Sales or "derivative" transactions, before or after the closing of this or future private placement transactions, may negatively impact the market price of the Company's publicly traded securities; (iii) any Purchaser, and counter-parties in "derivative" transactions to which any such Purchaser is a party, directly or indirectly, presently may have a "short" position in the Ordinary Shares, and (iv) each Purchaser shall not be deemed to have any affiliation with or control over any arm's length counter-party in any "derivative" transaction. The Company further understands and acknowledges that (y) one or more Purchasers may engage in hedging activities at various times during the period that the Securities are outstanding, and (z) such hedging activities (if any) could reduce the value of the existing shareholders' equity interests in the Company at and after the time that the hedging activities are being conducted. The Company acknowledges that such aforementioned hedging activities do not constitute a breach of any of the Transaction Documents.

(gg) Regulation M Compliance. The Company has not, and to its knowledge no one acting on its behalf has, (i) taken, directly or indirectly, any action designed to cause or to result in the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of any of the Securities, (ii) sold, bid for, purchased, or, paid any compensation for soliciting purchases of, any of the Securities, or (iii) paid or agreed to pay to any Person any compensation for soliciting another to purchase any other securities of the Company, other than, in the case of clauses (ii) and (iii), compensation paid to the Company's placement agent in connection with the placement of the Securities.

(hh) FDA. As to each product subject to the jurisdiction of the U.S. Food and Drug Administration ("FDA") under the Federal Food, Drug and Cosmetic Act, as amended, and the regulations thereunder ("FDCA") that is manufactured, packaged, labeled, tested, distributed, sold, and/or marketed by the Company or any of its Subsidiaries (each such product, a "Pharmaceutical Product"), such Pharmaceutical Product is being manufactured, packaged, labeled, tested, distributed, sold and/or marketed by the Company in compliance with all applicable requirements under FDCA and similar laws, rules and regulations relating to registration, investigational use, premarket clearance, licensure, or application approval, good manufacturing practices, good laboratory practices, good clinical practices, product listing, quotas, labeling, advertising, record keeping and filing of reports, except where the failure to be in compliance would not have a Material Adverse Effect. There is no pending, completed or, to the Company's knowledge, threatened, action (including any lawsuit, arbitration, or legal or administrative or regulatory proceeding, charge, complaint, or investigation) against the Company or any of its Subsidiaries, and none of the Company or any of its Subsidiaries has received any notice, warning letter or other communication from the FDA or any other governmental entity, which (i) contests the premarket clearance, licensure, registration, or approval of, the uses of, the distribution of, the manufacturing or packaging of, the testing of, the sale of, or the labeling and promotion of any Pharmaceutical Product, (ii) withdraws its approval of, requests the recall, suspension, or seizure of, or withdraws or orders the withdrawal of advertising or sales promotional

materials relating to, any Pharmaceutical Product, (iii) imposes a clinical hold on any clinical investigation by the Company or any of its Subsidiaries, (iv) enjoins production at any facility of the Company or any of its Subsidiaries, (v) enters or proposes to enter into a consent decree of permanent injunction with the Company or any of its Subsidiaries, or (vi) otherwise alleges any violation of any laws, rules or regulations by the Company or any of its Subsidiaries, and which in the case of each of the foregoing clauses (i) through (vi), either individually or in the aggregate, would reasonably be expected to have a Material Adverse Effect. The properties, business and operations of the Company have been and are being conducted in all material respects in accordance with all applicable laws, rules and regulations of the FDA. Except as disclosed in the SEC Reports, the Company has not been informed by the FDA that the FDA will prohibit the marketing, sale, license or use in the United States of any product proposed to be developed, produced or marketed by the Company nor has the FDA expressed any concern as to approving or clearing for marketing any product being developed or proposed to be developed by the Company.

(ii) Equity Plans. Each option granted by the Company under the Company's equity plan was granted (i) in accordance with the terms of the Company's equity plan and (ii) with an exercise price at least equal to the fair market value of the Ordinary Shares on the date such option would be considered granted under GAAP and applicable law. No option granted under the Company's equity plan has been backdated. The Company has not knowingly granted, and there is no and has been no Company policy or practice to knowingly grant, options prior to, or otherwise knowingly coordinate the grant of options with, the release or other public announcement of material information regarding the Company or its Subsidiaries or their financial results or prospects.

(jj) Office of Foreign Assets Control. Neither the Company nor any Subsidiary nor, to the Company's knowledge, any director, officer, agent, employee or affiliate of the Company or any Subsidiary is currently subject to any U.S. sanctions administered by the Office of Foreign Assets Control of the U.S. Treasury Department ("OFAC").

(kk) U.S. Real Property Holding Corporation. The Company is not and has never been a U.S. real property holding corporation within the meaning of Section 897 of the Internal Revenue Code of 1986, as amended.

(ll) Bank Holding Company Act. Neither the Company nor any of its Subsidiaries nor, to the Company's knowledge, any of its Affiliates is subject to the Bank Holding Company Act of 1956, as amended (the "BHCA") and to regulation by the Board of Governors of the Federal Reserve System (the "Federal Reserve"). Neither the Company nor any of its Subsidiaries nor, to the Company's knowledge, any of its Affiliates owns or controls, directly or indirectly, five percent (5%) or more of the outstanding shares of any class of voting securities or twenty-five percent (25%) or more of the total equity of a bank or any entity that is subject to the BHCA and to regulation by the Federal Reserve. Neither the Company nor any of its Subsidiaries nor, to the Company's knowledge, any of its Affiliates exercises a controlling influence over the management or policies of a bank or any entity that is subject to the BHCA and to regulation by the Federal Reserve.

(mm) Money Laundering. The operations of the Company and its Subsidiaries are and have been conducted at all times in compliance with applicable financial record-keeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, applicable money laundering statutes and applicable rules and regulations thereunder (collectively, the "Money Laundering Laws"), and no Action or Proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any Subsidiary with respect to the Money Laundering Laws is pending or, to the knowledge of the Company or any Subsidiary, threatened.

3.2 Representations and Warranties of the Purchasers. Each Purchaser, for itself and for no other Purchaser, hereby represents and warrants as of the date hereof and as of the Closing Date to the Company as follows (unless as of a specific date therein, in which case they shall be accurate as of such date):

(a) Organization; Authority. Such Purchaser is an entity duly incorporated or formed, validly existing and in good standing under the laws of the jurisdiction of its incorporation or formation with full right, corporate, partnership, limited liability company or similar power and authority to enter into and to consummate the transactions contemplated by the Transaction Documents and otherwise to carry out its obligations hereunder and thereunder. The execution and delivery of the Transaction Documents and performance by such Purchaser of the transactions contemplated by the Transaction Documents have been duly authorized by all necessary corporate, partnership, limited liability company or similar action, as applicable, on the part of such Purchaser. Each Transaction Document to which it is a party has been duly executed by such Purchaser, and when delivered by such Purchaser in accordance with the terms hereof, will constitute the valid and legally binding obligation of such Purchaser, enforceable against it in accordance with its terms, except: (i) as limited by general equitable principles and applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting enforcement of creditors' rights generally, (ii) as limited by laws relating to the availability of specific performance, injunctive relief or other equitable remedies and (iii) insofar as indemnification and contribution provisions may be limited by applicable law.

(b) Understandings or Arrangements. Such Purchaser is acquiring the Securities as principal for its own account and has no direct or indirect arrangement or understandings with any other persons to distribute or regarding the distribution of such Securities (this representation and warranty not limiting such Purchaser's right to sell the Securities pursuant to the Registration Statement or otherwise in compliance with applicable federal and state securities laws). Such Purchaser is acquiring the Securities hereunder in the ordinary course of its business.

(c) Purchaser Status. At the time such Purchaser was offered the Securities, it was, and as of the date hereof it is either: (i) an "accredited investor" as defined in Rule 501(a)(1), (a)(2), (a)(3), (a)(7), (a)(8), (a)(9), (a)(12), or (a)(13) under the Securities Act or (ii) a "qualified institutional buyer" as defined in Rule 144A(a) under the Securities Act.

(d) Experience of Such Purchaser. Such Purchaser, either alone or together with its representatives, has such knowledge, sophistication and experience in business and

financial matters so as to be capable of evaluating the merits and risks of the prospective investment in the Securities, and has so evaluated the merits and risks of such investment. Such Purchaser is able to bear the economic risk of an investment in the Securities and, at the present time, is able to afford a complete loss of such investment.

(e) Access to Information. Such Purchaser acknowledges that it has had the opportunity to review the Transaction Documents (including all exhibits and schedules thereto) and the SEC Reports and has been afforded, (i) the opportunity to ask such questions as it has deemed necessary of, and to receive answers from, representatives of the Company concerning the terms and conditions of the offering of the Securities and the merits and risks of investing in the Securities; (ii) access to information about the Company and its financial condition, results of operations, business, properties, management and prospects sufficient to enable it to evaluate its investment; and (iii) the opportunity to obtain such additional information that the Company possesses or can acquire without unreasonable effort or expense that is necessary to make an informed investment decision with respect to the investment. Such Purchaser acknowledges and agrees that neither the Placement Agent nor any Affiliate of the Placement Agent has provided such Purchaser with any information or advice with respect to the Securities nor is such information or advice necessary or desired. Neither the Placement Agent nor any Affiliate has made or makes any representation as to the Company or the quality of the Securities and the Placement Agent and any Affiliate may have acquired non-public information with respect to the Company which such Purchaser agrees need not be provided to it. In connection with the issuance of the Securities to such Purchaser, neither the Placement Agent nor any of its Affiliates has acted as a financial advisor or fiduciary to such Purchaser.

(f) Certain Transactions and Confidentiality. Other than consummating the transactions contemplated hereunder, such Purchaser has not, nor has any Person acting on behalf of or pursuant to any understanding with such Purchaser, directly or indirectly executed any purchases or sales, including Short Sales, of the securities of the Company during the period commencing as of the time that such Purchaser first received notice of the transaction contemplated hereunder (written or oral) from the Company or any other Person representing the Company and ending immediately prior to the execution hereof. Notwithstanding the foregoing, in the case of a Purchaser that is a multi-managed investment vehicle whereby separate portfolio managers manage separate portions of such Purchaser's assets and the portfolio managers have no direct knowledge of the investment decisions made by the portfolio managers managing other portions of such Purchaser's assets, the representation set forth above shall only apply with respect to the portion of assets managed by the portfolio manager that made the investment decision to purchase the Securities covered by this Agreement. Other than to other Persons party to this Agreement or to such Purchaser's representatives, including, without limitation, its officers, directors, partners, legal and other advisors, employees, agents and Affiliates, such Purchaser has maintained the confidentiality of all disclosures made to it in connection with this transaction (including the existence and terms of this transaction).

(g) Purchaser Independence. Such Purchaser acknowledges that such Purchaser is acting independently of any other Purchaser (other than with respect to an Affiliate of such Purchaser that is also a Purchaser hereunder) in connection with the

purchase of the Securities hereunder and is not acting in concert with any other Purchaser (other than with respect to an Affiliate of such Purchaser that is also a Purchaser hereunder) for the purposes of the Irish Takeover Panel Act 1997, Takeover Rules, 2013, and that no individual Purchaser or group of Purchasers acting in concert will own 30% or more of the Company's issued share capital on the Closing Date.

The Company acknowledges and agrees that the representations contained in this Section 3.2 shall not modify, amend or affect such Purchaser's right to rely on the Company's representations and warranties contained in this Agreement or any representations and warranties contained in any other Transaction Document or any other document or instrument executed and/or delivered in connection with this Agreement or the consummation of the transactions contemplated hereby. Notwithstanding the foregoing, for the avoidance of doubt, nothing contained herein shall constitute a representation or warranty, or preclude any actions, with respect to locating or borrowing shares in order to effect Short Sales or similar transactions in the future.

ARTICLE IV.
OTHER AGREEMENTS OF THE PARTIES

4.1 Furnishing of Information . Until the time that no Purchaser owns Securities, the Company covenants to timely file (or obtain extensions in respect thereof and file within the applicable grace period) all reports required to be filed by the Company after the date hereof pursuant to the Exchange Act even if the Company is not then subject to the reporting requirements of the Exchange Act.

4.2 Integration. The Company shall not sell, offer for sale or solicit offers to buy or otherwise negotiate in respect of any security (as defined in Section 2 of the Securities Act) that would be integrated with the offer or sale of the Securities for purposes of the rules and regulations of any Trading Market such that it would require shareholder approval prior to the closing of such other transaction unless shareholder approval is obtained before the closing of such subsequent transaction.

4.3 Securities Laws Disclosure; Publicity. The Company shall (a) by the Disclosure Time, issue a press release disclosing the material terms of the transactions contemplated hereby, and (b) file a Current Report on Form 8-K, including the Transaction Documents as exhibits thereto, with the Commission within the time required by the Exchange Act. From and after the issuance of such press release, the Company represents to the Purchasers that it shall have publicly disclosed all material, non-public information delivered to any of the Purchasers by the Company or any of its Subsidiaries, or any of their respective officers, directors, employees or agents in connection with the transactions contemplated by the Transaction Documents. In addition, effective upon the issuance of such press release, the Company acknowledges and agrees that any and all confidentiality or similar obligations under any agreement, whether written or oral, between the Company, any of its Subsidiaries or any of their respective officers, directors, agents, employees or Affiliates on the one hand, and any of the Purchasers or any of their Affiliates on the other hand, shall terminate. Notwithstanding the foregoing, the Company shall not publicly disclose the name of any Purchaser, or include the name of any Purchaser in any filing with the Commission or any regulatory agency or Trading Market, without the prior

written consent of such Purchaser, except (a) as required by federal securities law in connection with the filing of final Transaction Documents with the Commission and (b) to the extent such disclosure is required by law or Trading Market regulations, in which case the Company shall, to the extent permitted by law, provide the Purchasers with prior notice of such disclosure permitted under this clause (b).

4.4 Shareholder Rights Plan. No claim will be made or enforced by the Company or, with the consent of the Company, any other Person, that any Purchaser is an "Acquiring Person" under any control share acquisition, business combination, poison pill (including any distribution under a rights agreement) or similar anti-takeover plan or arrangement in effect or hereafter adopted by the Company, or that any Purchaser could be deemed to trigger the provisions of any such plan or arrangement, by virtue of receiving Securities under the Transaction Documents or under any other agreement between the Company and the Purchasers.

4.5 Non-Public Information. Except with respect to the material terms and conditions of the transactions contemplated by the Transaction Documents, which shall be disclosed pursuant to Section 4.3, the Company covenants and agrees that neither it, nor any other Person acting on its behalf will provide any Purchaser or its agents or counsel with any information that constitutes, or the Company reasonably believes constitutes, material non-public information, unless prior thereto such Purchaser shall have consented to the receipt of such information and agreed with the Company to keep such information confidential. The Company understands and confirms that each Purchaser shall be relying on the foregoing covenant in effecting transactions in securities of the Company. To the extent that the Company, any of its Subsidiaries, or any of their respective officers, directors, agents, employees or Affiliates, in any case acting on behalf of the Company or any of its Subsidiaries, delivers any material, non-public information to a Purchaser without such Purchaser's consent, the Company hereby covenants and agrees that such Purchaser shall not have any duty of confidentiality to the Company, any of its Subsidiaries, or any of their respective officers, directors, agents, employees or Affiliates, or a duty to the Company, any of its Subsidiaries or any of their respective officers, directors, agents, employees or Affiliates not to trade on the basis of, such material, non-public information, provided that the Purchaser shall remain subject to applicable law. Unless otherwise agreed by the applicable parties, to the extent that any notice provided pursuant to any Transaction Document constitutes, or contains, material, non-public information regarding the Company or any Subsidiaries, the Company shall simultaneously file such material non-public information with the Commission pursuant to a Current Report on Form 8-K. The Company understands and confirms that each Purchaser shall be relying on the foregoing covenant in effecting transactions in securities of the Company.

4.6 Use of Proceeds. Except as set forth in the Prospectus Supplement, the Company shall use the net proceeds from the issuance and sale of the Securities hereunder for general corporate purposes and shall not use such proceeds: (a) for the acquisition of any Ordinary Shares or Ordinary Share Equivalents, (b) for the settlement of any outstanding litigation or (c) in violation of FCPA or OFAC regulations.

4.7 Indemnification of Purchasers. Subject to the provisions of this Section 4.7, the Company will indemnify and hold each Purchaser and its directors, officers, shareholders, members, partners, employees and agents (and any other Persons with a functionally equivalent

role of a Person holding such titles notwithstanding a lack of such title or any other title), each Person who controls such Purchaser (within the meaning of Section 15 of the Securities Act and Section 20 of the Exchange Act), and the directors, officers, shareholders, agents, members, partners or employees (and any other Persons with a functionally equivalent role of a Person holding such titles notwithstanding a lack of such title or any other title) of such controlling persons (each, a "Purchaser Party") harmless from any and all losses, liabilities, obligations, claims, contingencies, damages, costs and expenses, including all judgments, amounts paid in settlements, court costs and reasonable attorneys' fees and costs of investigation that any such Purchaser Party may suffer or incur as a result of or relating to (a) any breach of any of the representations, warranties, covenants or agreements made by the Company in this Agreement or in the other Transaction Documents or (b) any action instituted against the Purchaser Parties in any capacity, or any of them or their respective Affiliates, by any shareholder of the Company who is not an Affiliate of such Purchaser Party, with respect to any of the transactions contemplated by the Transaction Documents (unless such action is solely based upon a material breach of such Purchaser Party's representations, warranties or covenants under the Transaction Documents or any agreements or understandings such Purchaser Party may have with any such shareholder or any violations by such Purchaser Party of state or federal securities laws or any conduct by such Purchaser Party which is finally judicially determined to constitute fraud, gross negligence or willful misconduct). If any action shall be brought against any Purchaser Party in respect of which indemnity may be sought pursuant to this Agreement, such Purchaser Party shall promptly notify the Company in writing, and the Company shall have the right to assume the defense thereof with counsel of its own choosing reasonably acceptable to the Purchaser Party. Any Purchaser Party shall have the right to employ separate counsel in any such action and participate in the defense thereof, but the fees and expenses of such counsel shall be at the expense of such Purchaser Party except to the extent that (i) the employment thereof has been specifically authorized by the Company in writing, (ii) the Company has failed after a reasonable period of time to assume such defense and to employ counsel or (iii) in such action there is, in the reasonable opinion of counsel, a material conflict on any material issue between the position of the Company and the position of such Purchaser Party, in which case the Company shall be responsible for the reasonable fees and expenses of no more than one such separate counsel. The Company will not be liable to any Purchaser Party under this Agreement (y) for any settlement by a Purchaser Party effected without the Company's prior written consent, which shall not be unreasonably withheld or delayed; or (z) to the extent, but only to the extent that a loss, claim, damage or liability is attributable to any Purchaser Party's breach of any of the representations, warranties, covenants or agreements made by such Purchaser Party in this Agreement or in the other Transaction Documents. The indemnification required by this Section 4.7 shall be made by periodic payments of the amount thereof during the course of the investigation or defense, as and when bills are received or are incurred. The indemnity agreements contained herein shall be in addition to any cause of action or similar right of any Purchaser Party against the Company or others and any liabilities the Company may be subject to pursuant to law.

4.8 Listing of Ordinary Shares . The Company hereby agrees to use commercially reasonable best efforts to maintain the listing or quotation of the Ordinary Shares on the Trading Market on which the Ordinary Shares are currently listed, and concurrently with the Closing, the Company shall apply to list or quote all of the Shares on such Trading Market and promptly secure the listing of all of the Shares on such Trading Market. The Company further agrees, if the Company applies to have the Ordinary Shares traded on any other Trading Market, it will

then include in such application all of the Shares, and will take such other action as is necessary to cause all of the Shares to be listed or quoted on such other Trading Market as promptly as possible. The Company will then take all action reasonably necessary to continue the listing and trading of its Ordinary Shares on a Trading Market and will comply in all respects with the Company's reporting, filing and other obligations under the bylaws or rules of the Trading Market. The Company agrees to maintain the eligibility of the Ordinary Shares for electronic transfer through the Depository Trust Company or another established clearing corporation, including, without limitation, by timely payment of fees to the Depository Trust Company or such other established clearing corporation in connection with such electronic transfer.

4.9 Reservation of Ordinary Shares.. As of the date hereof, the Company has reserved and the Company shall continue to reserve, a sufficient number of Ordinary Shares for the purpose of enabling the Company to issue Shares pursuant to this Agreement.

4.10 Subsequent Equity Sales .

(a) From the date hereof until thirty (30) days after the Closing Date, neither the Company nor any Subsidiary shall issue, enter into any agreement to issue or announce the issuance or proposed issuance of any shares of Ordinary Shares or Ordinary Share Equivalents.

(b) From the date hereof until the one (1) year anniversary of the Closing Date, the Company shall be prohibited from effecting or entering into an agreement to effect any issuance by the Company or any of its Subsidiaries of Ordinary Shares or Ordinary Share Equivalents (or a combination of units thereof) involving a Variable Rate Transaction. " Variable Rate Transaction" means a transaction in which the Company (i) issues or sells any debt or equity securities that are convertible into, exchangeable or exercisable for, or include the right to receive additional shares of Ordinary Shares either (A) at a conversion price, exercise price or exchange rate or other price that is based upon and/or varies with the trading prices of or quotations for the shares of Ordinary Shares at any time after the initial issuance of such debt or equity securities, or (B) with a conversion, exercise or exchange price that is subject to being reset at some future date after the initial issuance of such debt or equity security or upon the occurrence of specified or contingent events directly or indirectly related to the business of the Company or the market for the Ordinary Shares or (ii) enters into, or effects a transaction under, any agreement, including, but not limited to, an equity line of credit, whereby the Company may issue securities at a future determined price ; provided, however, that an "at the market" offering pursuant to an "at the market" equity distribution or sales agreement with the Placement Agent shall not constitute a "Variable Rate Transaction." Any Purchaser shall be entitled to obtain injunctive relief against the Company to preclude any such issuance, which remedy shall be in addition to any right to collect damages.

(c) Notwithstanding the foregoing, this Section 4.10 shall not apply in respect of an Exempt Issuance, except that no Variable Rate Transaction shall be an Exempt Issuance.

4.11 Equal Treatment of Purchasers. No consideration (including any modification of any Transaction Document) shall be offered or paid to any Person to amend or consent to a waiver or modification of any provision of the Transaction Documents unless the same consideration is also offered to all of the parties to the Transaction Documents. For clarification purposes, this provision constitutes a separate right granted to each Purchaser by the Company and negotiated separately by each Purchaser, and is intended for the Company to treat the Purchasers as a class and shall not in any way be construed as the Purchasers acting in concert or as a group with respect to the purchase, disposition or voting of Securities or otherwise.

4.12 Certain Transactions and Confidentiality. Each Purchaser, severally and not jointly with the other Purchasers, covenants that neither it nor any Affiliate acting on its behalf or pursuant to any understanding with it will execute any purchases or sales, including Short Sales of any of the Company's securities during the period commencing with the execution of this Agreement and ending at such time that the transactions contemplated by this Agreement are first publicly announced pursuant to the initial press release as described in Section 4.3. Each Purchaser, severally and not jointly with the other Purchasers, covenants that until such time as the transactions contemplated by this Agreement are publicly disclosed by the Company pursuant to the initial press release as described in Section 4.3, such Purchaser will maintain the confidentiality of the existence and terms of this transaction and the information included in the Disclosure Schedules. Notwithstanding the foregoing, and notwithstanding anything contained in this Agreement to the contrary, the Company expressly acknowledges and agrees that (i) no Purchaser makes any representation, warranty or covenant hereby that it will not engage in effecting transactions in any securities of the Company after the time that the transactions contemplated by this Agreement are first publicly announced pursuant to the initial press release as described in Section 4.3, (ii) no Purchaser shall be restricted or prohibited from effecting any transactions in any securities of the Company in accordance with applicable securities laws from and after the time that the transactions contemplated by this Agreement are first publicly announced pursuant to the initial press release as described in Section 4.3 and (iii) no Purchaser shall have any duty of confidentiality or duty not to trade in the securities of the Company to the Company or its Subsidiaries after the issuance of the initial press release as described in Section 4.3. Notwithstanding the foregoing, in the case of a Purchaser that is a multi-managed investment vehicle whereby separate portfolio managers manage separate portions of such Purchaser's assets and the portfolio managers have no direct knowledge of the investment decisions made by the portfolio managers managing other portions of such Purchaser's assets, the covenant set forth above shall only apply with respect to the portion of assets managed by the portfolio manager that made the investment decision to purchase the Securities covered by this Agreement.

4.13 Lock-Up Agreements. The Company shall not amend, modify, waive or terminate any provision of any of the Lock-Up Agreements except to extend the term of the lock-up period and shall enforce the provisions of each Lock-Up Agreement in accordance with its terms. If any party to a Lock-Up Agreement breaches any provision of a Lock-Up Agreement, the Company shall promptly use its best efforts to seek specific performance of the terms of such Lock-Up Agreement.

ARTICLE V.
MISCELLANEOUS

5.1 Termination. This Agreement may be terminated by any Purchaser, as to such Purchaser's obligations hereunder only and without any effect whatsoever on the obligations between the Company and the other Purchasers, by written notice to the other parties, if the Closing has not been consummated on or before the fifth (5th) Trading Day following the date hereof; provided, however, that no such termination will affect the right of any party to sue for any breach by any other party (or parties).

5.2 Fees and Expenses. Except as expressly set forth in the Transaction Documents to the contrary, each party shall pay the fees and expenses of its advisers, counsel, accountants and other experts, if any, and all other expenses incurred by such party incident to the negotiation, preparation, execution, delivery and performance of this Agreement. The Company shall pay, or procure payment of, all Transfer Agent fees (including, without limitation, any fees required for same-day processing of any instruction letter delivered by the Company and any exercise notice delivered by a Purchaser) in connection with the delivery of any Securities to the Purchasers pursuant to this Agreement. The Company shall use its best efforts to pay, or procure payment of stamp taxes and other taxes and duties levied in connection with the delivery of any Securities to the Purchasers pursuant to this Agreement, save for any stamp taxes and other taxes and duties levied in connection with the delivery of any Pre-Settlement Shares ("Relevant Taxes"). Each Purchaser agrees to cooperate with the Company and provide all necessary information and documentation to the Company in a timely manner (and in any event within 15 Business Days of request) to enable the Company to procure payment of any Relevant Taxes and facilitate the making of any necessary filings in respect of Relevant Taxes required to be made within applicable time limits. The Company shall not be liable for any Relevant Taxes or any penalty, fine, surcharge, interest, charge, cost or other similar imposition arising in respect of Relevant Taxes to the extent that such amount arises or is increased as a result of any failure by a Purchaser to timely provide the Company with any information or documentation requested pursuant to this Section 5.2.

5.3 Entire Agreement. The Transaction Documents, together with the exhibits and schedules thereto, the Prospectus and the Prospectus Supplement, contain the entire understanding of the parties with respect to the subject matter hereof and thereof and supersede all prior agreements and understandings, oral or written, with respect to such matters, which the parties acknowledge have been merged into such documents, exhibits and schedules.

5.4 Notices. Any and all notices or other communications or deliveries required or permitted to be provided hereunder shall be in writing and shall be deemed given and effective on the earliest of: (a) the time of transmission, if such notice or communication is delivered via facsimile at the facsimile number or email attachment at the email address as set forth on the signature pages attached hereto at or prior to 5:30 p.m. (New York City time) on a Trading Day, (b) the next Trading Day after the time of transmission, if such notice or communication is delivered via facsimile at the facsimile number or email attachment at the email address as set forth on the signature pages attached hereto on a day that is not a Trading Day or later than 5:30 p.m. (New York City time) on any Trading Day, (c) the second (2nd) Trading Day following the date of mailing, if sent by U.S. nationally recognized overnight courier service or (d) upon actual

receipt by the party to whom such notice is required to be given. The address for such notices and communications shall be as set forth on the signature pages attached hereto. Unless otherwise agreed by the applicable parties, to the extent that any notice provided pursuant to any Transaction Document constitutes, or contains, material, non-public information regarding the Company or any Subsidiaries, the Company shall simultaneously file such material non-public information with the Commission pursuant to a Current Report on Form 8-K.

5.5 Amendments; Waivers. No provision of this Agreement may be waived, modified, supplemented or amended except in a written instrument signed, in the case of an amendment, by the Company and Purchasers which purchased pursuant to this Agreement at least 50.1% in interest of the Shares based on the initial Subscription Amounts hereunder or, in the case of a waiver, by the party against whom enforcement of any such waived provision is sought, provided that if any amendment, modification or waiver disproportionately and adversely impacts a Purchaser (or group of Purchasers), the consent of such disproportionately impacted Purchaser (or group of Purchasers) shall also be required. No waiver of any default with respect to any provision, condition or requirement of this Agreement shall be deemed to be a continuing waiver in the future or a waiver of any subsequent default or a waiver of any other provision, condition or requirement hereof, nor shall any delay or omission of any party to exercise any right hereunder in any manner impair the exercise of any such right. Any proposed amendment or waiver that disproportionately, materially and adversely affects the rights and obligations of any Purchaser relative to the comparable rights and obligations of the other Purchasers shall require the prior written consent of such adversely affected Purchaser. Any amendment effected in accordance with this Section 5.5 shall be binding upon each Purchaser and holder of Securities and the Company.

5.6 Headings. The headings herein are for convenience only, do not constitute a part of this Agreement and shall not be deemed to limit or affect any of the provisions hereof.

5.7 Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of the parties and their successors and permitted assigns. The Company may not assign this Agreement or any rights or obligations hereunder without the prior written consent of each Purchaser (other than by merger). Any Purchaser may assign any or all of its rights under this Agreement to any Person to whom such Purchaser assigns or transfers any Securities, provided that such transferee agrees in writing to be bound, with respect to the transferred Securities, by the provisions of the Transaction Documents that apply to the "Purchasers", provided that, in connection with any such assignment of any rights under this Agreement prior to the Closing Date (other than any assignment to an Affiliate of such Purchaser, for which no consent shall be required), such assignment shall require the prior written consent of the Company, which consent shall not be unreasonably withheld.

5.8 No Third-Party Beneficiaries. The Placement Agent shall be the third party beneficiary of the representations and warranties of the Company in Section 3.1 and the representations and warranties of the Purchasers in Section 3.2. This Agreement is intended for the benefit of the parties hereto and their respective successors and permitted assigns and is not for the benefit of, nor may any provision hereof be enforced by, any other Person, except as otherwise set forth in Section 4.7 and this Section 5.8.

5.9 Governing Law. All questions concerning the construction, validity, enforcement and interpretation of the Transaction Documents shall be governed by and construed and enforced in accordance with the internal laws of the State of New York, without regard to the principles of conflicts of law thereof. Each party agrees that all legal Proceedings concerning the interpretations, enforcement and defense of the transactions contemplated by this Agreement and any other Transaction Documents (whether brought against a party hereto or its respective affiliates, directors, officers, shareholders, partners, members, employees or agents) shall be commenced exclusively in the state and federal courts sitting in the City of New York. Each party hereby irrevocably submits to the exclusive jurisdiction of the state and federal courts sitting in the City of New York, Borough of Manhattan for the adjudication of any dispute hereunder or in connection herewith or with any transaction contemplated hereby or discussed herein (including with respect to the enforcement of any of the Transaction Documents), and hereby irrevocably waives, and agrees not to assert in any Action or Proceeding, any claim that it is not personally subject to the jurisdiction of any such court, that such Action or Proceeding is improper or is an inconvenient venue for such Proceeding. Each party hereby irrevocably waives personal service of process and consents to process being served in any such Action or Proceeding by mailing a copy thereof via registered or certified mail or overnight delivery (with evidence of delivery) to such party at the address in effect for notices to it under this Agreement and agrees that such service shall constitute good and sufficient service of process and notice thereof. Nothing contained herein shall be deemed to limit in any way any right to serve process in any other manner permitted by law. If any party shall commence an Action or Proceeding to enforce any provisions of the Transaction Documents, then, in addition to the obligations of the Company under Section 4.7, the prevailing party in such Action or Proceeding shall be reimbursed by the non-prevailing party for its reasonable attorneys' fees and other costs and expenses incurred with the investigation, preparation and prosecution of such Action or Proceeding.

5.10 Survival. The representations and warranties contained herein shall survive the Closing and the delivery of the Securities for two (2) years following the Closing Date.

5.11 Execution. This Agreement may be executed in two or more counterparts, all of which when taken together shall be considered one and the same agreement and shall become effective when counterparts have been signed by each party and delivered to each other party, it being understood that the parties need not sign the same counterpart. In the event that any signature is delivered by facsimile transmission or by e-mail delivery of a ".pdf" format data file, such signature shall create a valid and binding obligation of the party executing (or on whose behalf such signature is executed) with the same force and effect as if such facsimile or ".pdf" signature page were an original thereof.

5.12 Severability. If any term, provision, covenant or restriction of this Agreement is held by a court of competent jurisdiction to be invalid, illegal, void or unenforceable, the remainder of the terms, provisions, covenants and restrictions set forth herein shall remain in full force and effect and shall in no way be affected, impaired or invalidated, and the parties hereto shall use their commercially reasonable efforts to find and employ an alternative means to achieve the same or substantially the same result as that contemplated by such term, provision, covenant or restriction. It is hereby stipulated and declared to be the intention of the parties that

they would have executed the remaining terms, provisions, covenants and restrictions without including any of such that may be hereafter declared invalid, illegal, void or unenforceable.

5.13 Rescission and Withdrawal Right. Notwithstanding anything to the contrary contained in (and without limiting any similar provisions of) any of the other Transaction Documents, whenever any Purchaser exercises a right, election, demand or option under a Transaction Document and the Company does not timely perform its related obligations within the periods therein provided, then such Purchaser may rescind or withdraw, in its sole discretion from time to time upon written notice to the Company, any relevant notice, demand or election in whole or in part without prejudice to its future actions and rights.

5.14 Replacement of Securities. If any certificate or instrument evidencing any Securities is mutilated, lost, stolen or destroyed, the Company shall issue or cause to be issued in exchange and substitution for and upon cancellation thereof (in the case of mutilation), or in lieu of and substitution therefor, a new certificate or instrument, but only upon receipt of evidence reasonably satisfactory to the Company of such loss, theft or destruction. The applicant for a new certificate or instrument under such circumstances shall also pay any reasonable third-party costs (including customary indemnity) associated with the issuance of such replacement Securities.

5.15 Remedies. In addition to being entitled to exercise all rights provided herein or granted by law, including recovery of damages, each of the Purchasers and the Company will be entitled to specific performance under the Transaction Documents. The parties agree that monetary damages may not be adequate compensation for any loss incurred by reason of any breach of obligations contained in the Transaction Documents and hereby agree to waive and not to assert in any Action for specific performance of any such obligation the defense that a remedy at law would be adequate.

5.16 Payment Set Aside. To the extent that the Company makes a payment or payments to any Purchaser pursuant to any Transaction Document or a Purchaser enforces or exercises its rights thereunder, and such payment or payments or the proceeds of such enforcement or exercise or any part thereof are subsequently invalidated, declared to be fraudulent or preferential, set aside, recovered from, disgorged by or are required to be refunded, repaid or otherwise restored to the Company, a trustee, receiver or any other Person under any law (including, without limitation, any bankruptcy law, state or federal law, common law or equitable cause of action), then to the extent of any such restoration the obligation or part thereof originally intended to be satisfied shall be revived and continued in full force and effect as if such payment had not been made or such enforcement or setoff had not occurred.

5.17 Independent Nature of Purchasers' Obligations and Rights. The obligations of each Purchaser under any Transaction Document are several and not joint with the obligations of any other Purchaser, and no Purchaser shall be responsible in any way for the performance or non-performance of the obligations of any other Purchaser under any Transaction Document. Nothing contained herein or in any other Transaction Document, and no action taken by any Purchaser pursuant hereto or thereto, shall be deemed to constitute the Purchasers as a partnership, an association, a joint venture or any other kind of entity, or create a presumption that the Purchasers are in any way acting in concert or as a group with respect to such obligations

or the transactions contemplated by the Transaction Documents. Each Purchaser shall be entitled to independently protect and enforce its rights including, without limitation, the rights arising out of this Agreement or out of the other Transaction Documents, and it shall not be necessary for any other Purchaser to be joined as an additional party in any Proceeding for such purpose. Each Purchaser has been represented by its own separate legal counsel in its review and negotiation of the Transaction Documents. For reasons of administrative convenience only, each Purchaser and its respective counsel have chosen to communicate with the Company through the legal counsel of the Placement Agent. The legal counsel of the Placement Agent does not represent any of the Purchasers and only represents the Placement Agent. The Company has elected to provide all Purchasers with the same terms and Transaction Documents for the convenience of the Company and not because it was required or requested to do so by any of the Purchasers. It is expressly understood and agreed that each provision contained in this Agreement and in each other Transaction Document is between the Company and a Purchaser, solely, and not between the Company and the Purchasers collectively and not between and among the Purchasers.

5.18 Liquidated Damages. The Company's obligations to pay any liquidated damages or other amounts owing under the Transaction Documents is a continuing obligation of the Company and shall not terminate until all unpaid liquidated damages and other amounts have been paid notwithstanding the fact that the instrument or security pursuant to which such liquidated damages or other amounts are due and payable shall have been canceled.

5.19 Saturdays, Sundays, Holidays, etc. If the last or appointed day for the taking of any action or the expiration of any right required or granted herein shall not be a Business Day, then such action may be taken or such right may be exercised on the next succeeding Business Day.

5.20 Construction. The parties agree that each of them and/or their respective counsel have reviewed and had an opportunity to revise the Transaction Documents and, therefore, the normal rule of construction to the effect that any ambiguities are to be resolved against the drafting party shall not be employed in the interpretation of the Transaction Documents or any amendments thereto. In addition, each and every reference to share prices and Ordinary Shares in any Transaction Document shall be subject to adjustment for reverse and forward share splits, share dividends, share combinations and other similar transactions of the Ordinary Shares that occur after the date of this Agreement.

5.21 **WAIVER OF JURY TRIAL . IN ANY ACTION, SUIT, OR PROCEEDING IN ANY JURISDICTION BROUGHT BY ANY PARTY AGAINST ANY OTHER PARTY, THE PARTIES EACH KNOWINGLY AND INTENTIONALLY, TO THE GREATEST EXTENT PERMITTED BY APPLICABLE LAW, HEREBY ABSOLUTELY, UNCONDITIONALLY, IRREVOCABLY AND EXPRESSLY WAIVES FOREVER TRIAL BY JURY.**

(Signature Pages Follow)

IN WITNESS WHEREOF, the parties hereto have caused this Securities Purchase Agreement to be duly executed by their respective authorized signatories as of the date first indicated above.

Iterum Therapeutics plc

By: /s/ Corey Fishman
Name: Corey Fishman
Title: CEO

Address for Notice:

Fax:
E-mail:

With a copy to (which shall not constitute notice):

Wilmer Cutler Pickering Hale and Dorr LLP
7 World Trade Center
250 Greenwich Street
New York, New York 10007
Attn: Brian A. Johnson, Esq.
E-mail:
Facsimile: +1-212-230-8800

[REMAINDER OF PAGE INTENTIONALLY LEFT BLANK
SIGNATURE PAGE FOR PURCHASER FOLLOWS]

[PURCHASER SIGNATURE PAGES TO ITRM SECURITIES PURCHASE AGREEMENT]

IN WITNESS WHEREOF, the undersigned have caused this Securities Purchase Agreement to be duly executed by their respective authorized signatories as of the date first indicated above.

Name of Purchaser: __Alyeska Master Fund, L.P._____
Signature of Authorized Signatory of Purchaser: __/s/ Jason Bragg_____
Name of Authorized Signatory: _Jason Bragg_____
Title of Authorized Signatory: _CFO, Alyeska Investment Group, L.P._____
Email Address of Authorized Signatory: _[**]_____
Facsimile Number of Authorized Signatory: _[**]_____
Address for Notice to Purchaser: _[**]_____

Email address for Notice to Purchaser: _[**]_____

Address for Delivery of Securities to Purchaser (if not same as address for notice):

Subscription Amount: $4,000,000

Shares: 2,000,000

EIN Number: [**]

☐ Notwithstanding anything contained in this Agreement to the contrary, by checking this box (i) the obligations of the above-signed to purchase the securities set forth in this Agreement to be purchased from the Company by the above-signed, and the obligations of the Company to issue and sell such securities to the above-signed, shall be unconditional and all conditions to Closing shall be disregarded, (ii) the Closing shall occur on the second (2nd) Trading Day following the date of this Agreement and (iii) any condition to Closing contemplated by this Agreement (but prior to being disregarded by clause (i) above) that required delivery by the Company or the above-signed of any agreement, instrument, certificate or the like or purchase price (as applicable) shall no longer be a condition and shall instead be an unconditional obligation of the Company or the above-signed (as applicable) to deliver such agreement, instrument, certificate or the like or purchase price (as applicable) to such other party on the Closing Date.

[SIGNATURE PAGES CONTINUE]

[PURCHASER SIGNATURE PAGES TO ITRM SECURITIES PURCHASE AGREEMENT]

IN WITNESS WHEREOF, the undersigned have caused this Securities Purchase Agreement to be duly executed by their respective authorized signatories as of the date first indicated above.

Name of Purchaser: __FiveT Capital AG / FiveT Investment Management_____
Signature of Authorized Signatory of Purchaser: _/s/ Johannes Minho Roth_____
Name of Authorized Signatory: _Johannes Minho Roth _____
Title of Authorized Signatory: _Authorized Person_____
Email Address of Authorized Signatory:__[**]_____
Facsimile Number of Authorized Signatory: _[**]_____
Address for Notice to Purchaser: [**]

Email address for Notice to Purchaser:__[**]_____

Address for Delivery of Securities to Purchaser (if not same as address for notice):

Subscription Amount: $_7,750,000_____

Shares: _3,875,000_____

EIN Number: ___[**]_____

X Notwithstanding anything contained in this Agreement to the contrary, by checking this box (i) the obligations of the above-signed to purchase the securities set forth in this Agreement to be purchased from the Company by the above-signed, and the obligations of the Company to issue and sell such securities to the above-signed, shall be unconditional and all conditions to Closing shall be disregarded, (ii) the Closing shall occur on the second (2nd) Trading Day following the date of this Agreement and (iii) any condition to Closing contemplated by this Agreement (but prior to being disregarded by clause (i) above) that required delivery by the Company or the above-signed of any agreement, instrument, certificate or the like or purchase price (as applicable) shall no longer be a condition and shall instead be an unconditional obligation of the Company or the above-signed (as applicable) to deliver such agreement, instrument, certificate or the like or purchase price (as applicable) to such other party on the Closing Date.

[SIGNATURE PAGES CONTINUE]

[PURCHASER SIGNATURE PAGES TO ITRM SECURITIES PURCHASE AGREEMENT]

IN WITNESS WHEREOF, the undersigned have caused this Securities Purchase Agreement to be duly executed by their respective authorized signatories as of the date first indicated above.

Name of Purchaser: _CVI Investments, Inc., by Heights Capital Management, Inc., its authorized signatory_
Signature of Authorized Signatory of Purchaser: _/s/ Martin Kobinger_____
Name of Authorized Signatory: __Martin Kobinger_____
Title of Authorized Signatory: _Investment Manager_____
Email Address of Authorized Signatory: _[**]_____
Facsimile Number of Authorized Signatory: _____[**]_____
Address for Notice to Purchaser: c/o Heighs Capital Management, Inc., 101 California Street, Suite 3250, San Francisco, CA 94111

Email address for Notice to Purchaser:__[**]_____

Address for Delivery of Securities to Purchaser (if not same as address for notice):

Subscription Amount: $_7,750,000_____

Shares: _3,875,000_____

EIN Number: _[**]_____

☐ Notwithstanding anything contained in this Agreement to the contrary, by checking this box (i) the obligations of the above-signed to purchase the securities set forth in this Agreement to be purchased from the Company by the above-signed, and the obligations of the Company to issue and sell such securities to the above-signed, shall be unconditional and all conditions to Closing shall be disregarded, (ii) the Closing shall occur on the second (2nd) Trading Day following the date of this Agreement and (iii) any condition to Closing contemplated by this Agreement (but prior to being disregarded by clause (i) above) that required delivery by the Company or the above-signed of any agreement, instrument, certificate or the like or purchase price (as applicable) shall no longer be a condition and shall instead be an unconditional obligation of the Company or the above-signed (as applicable) to deliver such agreement, instrument, certificate or the like or purchase price (as applicable) to such other party on the Closing Date.

[SIGNATURE PAGES CONTINUE]

[PURCHASER SIGNATURE PAGES TO ITRM SECURITIES PURCHASE AGREEMENT]

IN WITNESS WHEREOF, the undersigned have caused this Securities Purchase Agreement to be duly executed by their respective authorized signatories as of the date first indicated above.

Name of Purchaser: _Sabby Volatility Warrant Master Fund, Ltd._____
Signature of Authorized Signatory of Purchaser: _/s/ Robert Grundstein_____
Name of Authorized Signatory: _Robert Grundstein_____
Title of Authorized Signatory: _COO of Purchaser's Investment Manager_____
Email Address of Authorized Signatory: _[**]_____
Facsimile Number of Authorized Signatory: ____[**]_____
Address for Notice to Purchaser: [**]

Email address for Notice to Purchaser:___[**]_____

Address for Delivery of Securities to Purchaser (if not same as address for notice):
[**]

Subscription Amount: $_15,500,000_____

Shares: _7,750,000_____

EIN Number: _[**]_____

☐ Notwithstanding anything contained in this Agreement to the contrary, by checking this box (i) the obligations of the above-signed to purchase the securities set forth in this Agreement to be purchased from the Company by the above-signed, and the obligations of the Company to issue and sell such securities to the above-signed, shall be unconditional and all conditions to Closing shall be disregarded, (ii) the Closing shall occur on the second (2nd) Trading Day following the date of this Agreement and (iii) any condition to Closing contemplated by this Agreement (but prior to being disregarded by clause (i) above) that required delivery by the Company or the above-signed of any agreement, instrument, certificate or the like or purchase price (as applicable) shall no longer be a condition and shall instead be an unconditional obligation of the Company or the above-signed (as applicable) to deliver such agreement, instrument, certificate or the like or purchase price (as applicable) to such other party on the Closing Date.

Exhibit 22.1

Subsidiary Issuers and Subsidiary Guarantors of Guaranteed Securities

Guaranteed Security	Subsidiary Issuer	Co-Guarantors
6.500% Exchangeable Senior Subordinated Notes due 2025	Iterum Therapeutics Bermuda Limited	•Iterum Therapeutics International Limited (subsidiary guarantor) •Iterum Therapeutics US Limited (subsidiary guarantor) •Iterum Therapeutics US Holding Limited (subsidiary guarantor) •Iterum Therapeutics plc (parent guarantor)
Limited Recourse Royalty-Linked Subordinated Notes	Iterum Therapeutics Bermuda Limited	•Iterum Therapeutics International Limited (subsidiary guarantor) •Iterum Therapeutics US Limited (subsidiary guarantor) •Iterum Therapeutics US Holding Limited (subsidiary guarantor) •Iterum Therapeutics plc (parent guarantor)

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Shareholders and Board of Directors
Iterum Therapeutics plc:

We consent to the incorporation by reference in the registration statements Nos. 333-225236, 333-230496, 333-237198 and 333-245655 on Form S-8 and No. 333-232569 on Form S-3 of Iterum Therapeutics plc of our report dated March 12, 2021, with respect to the consolidated balance sheets of Iterum Therapeutics plc as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, convertible preferred shares and shareholders' (deficit)/equity, and cash flows for each of the years in the three-year period ended December 31, 2020, and the related notes, which report appears in the December 31, 2020 annual report on Form 10-K of Iterum Therapeutics plc.

Our report on the consolidated financial statements refers to a change to the method of accounting for leases as of January 1, 2019 due to the adoption of ASC Topic 842, *Leases*.

/s/ KPMG

Dublin, Ireland
March 12, 2021

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Corey Fishman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Iterum Therapeutics plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2021

By: /s/ Corey Fishman

Corey Fishman
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Judith Matthews, certify that:

1. I have reviewed this Annual Report on Form 10-K of Iterum Therapeutics plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2021

By: /s/ Judith Matthews

Judith Matthews
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Iterum Therapeutics plc (the "Company") for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Corey Fishman, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to his knowledge on the date hereof:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 12, 2021

By: /s/ Corey Fishman

Corey Fishman
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Iterum Therapeutics plc (the "Company") for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Judith Matthews, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to her knowledge on the date hereof:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 12, 2021

By: /s/ Judith Matthews

Judith Matthews
Chief Financial Officer
(Principal Financial and Accounting Officer)