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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2019

OR

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

For the transition period from to

Commission File Number 001-38503

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

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

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

Not applicable
(Zip Code)

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

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

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

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

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

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

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

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PART I

Item 1. Business.

Overview

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

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

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

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

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

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

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

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

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

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

Sulopenem Program, Clinical and Regulatory Status

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

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

Our Strategy

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

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

The Medical Need

Urinary Tract and Intra-Abdominal Infections

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

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

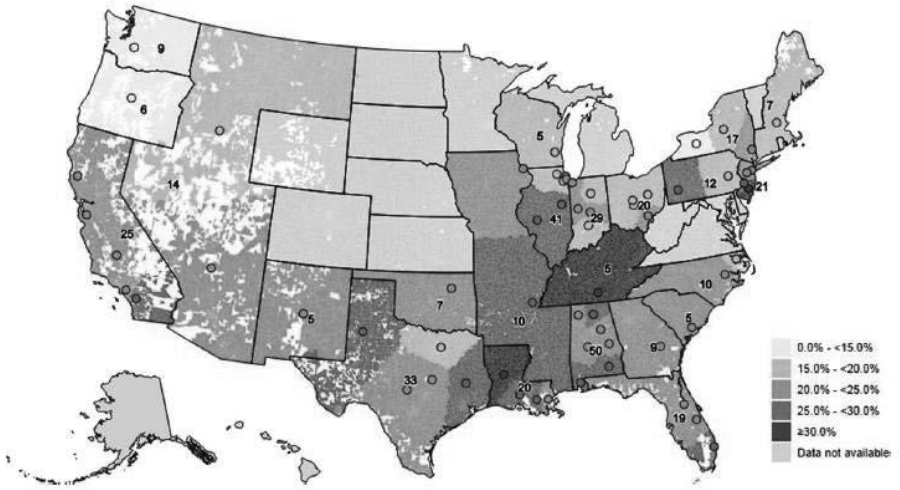
cIAIs have similar challenges to those of cUTIs. These complicated infections extend from a gastrointestinal source, such as the appendix or the colon, into the peritoneal space and can be associated with abscess formation.

Antimicrobial Resistance is Increasing

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

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

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



Numbers represent hospital centers from which data were derived

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

There is a Significant Population at Risk

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

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

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

Limited Treatment Options

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

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

The Challenge of Developing Antibiotics

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

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

The Solution to Rising Resistance

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

These new agents will need to:

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

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

Our Sulopenem Program

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

Potential Advantages of Oral Sulopenem and Sulopenem

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

Sulopenem's differentiating characteristics include:

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

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

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

Market Opportunity for Oral Sulopenem and Sulopenem

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

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

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

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

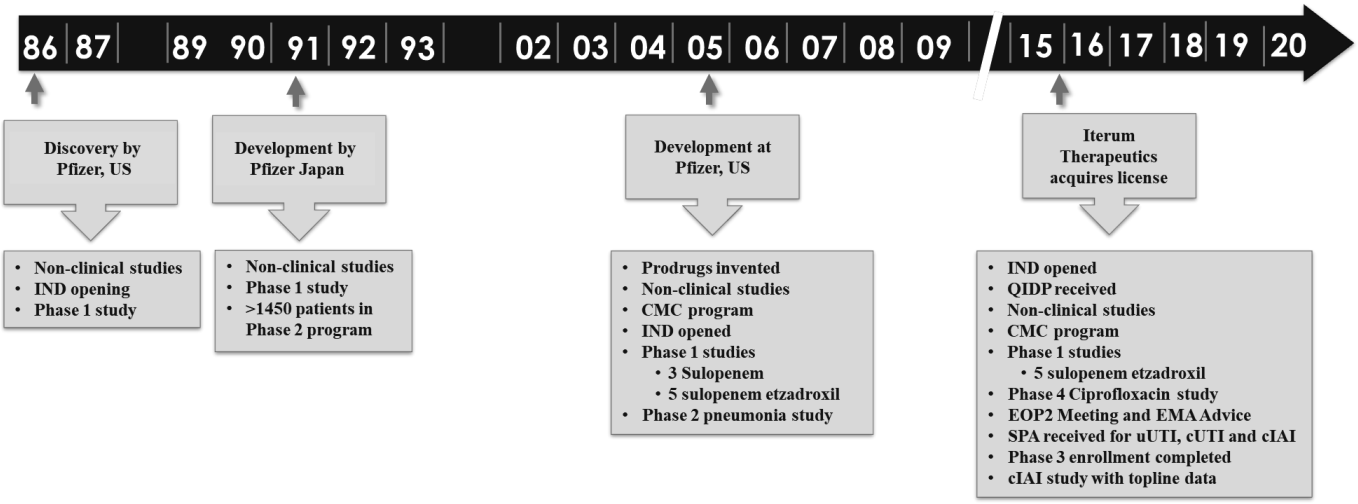
Given the growing prevalence of bacterial resistance that has rendered existing oral therapies ineffective, coupled with the FDA mandating new safety labeling changes to enhance warnings limiting fluoroquinolone use in uncomplicated infections due to the association with disabling and potentially permanent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

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

Oral Sulopenem and Sulopenem Clinical Development Program

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

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



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

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

Microbiology Surveillance Data

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

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

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

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

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

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

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

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

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

Animal Models

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

Non-clinical Pharmacology

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

Phase 1 Program

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

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

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

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

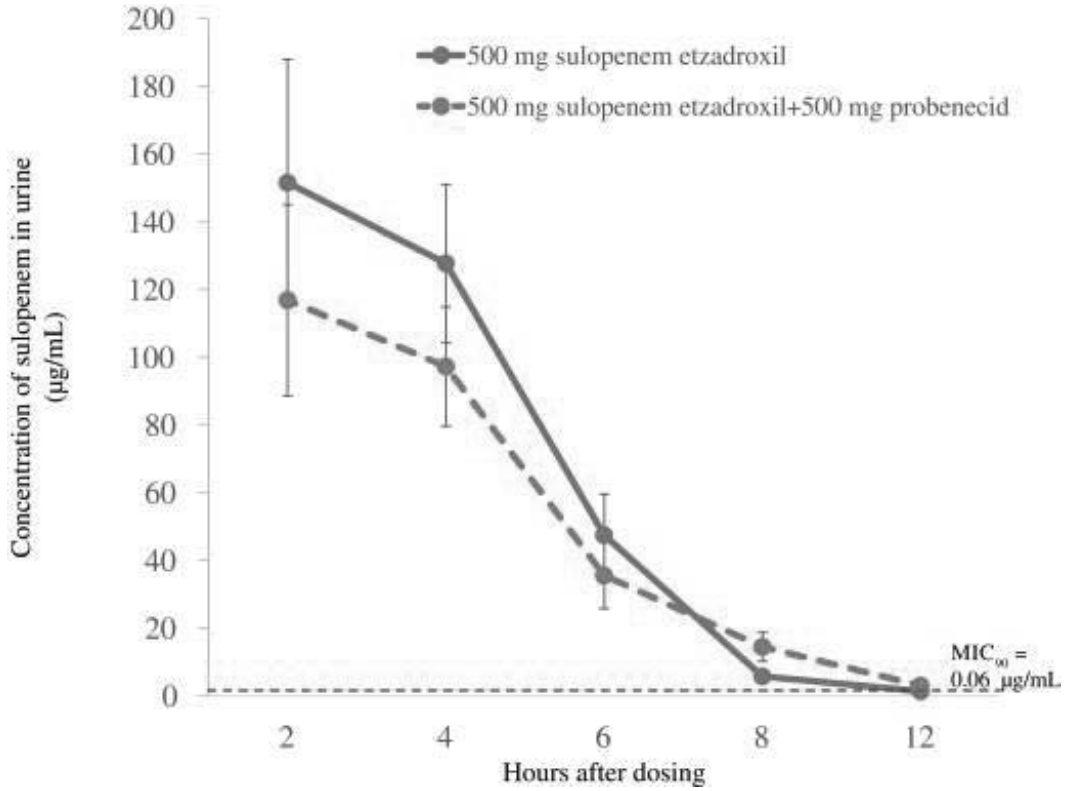
Oral Sulopenem

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

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

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

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



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

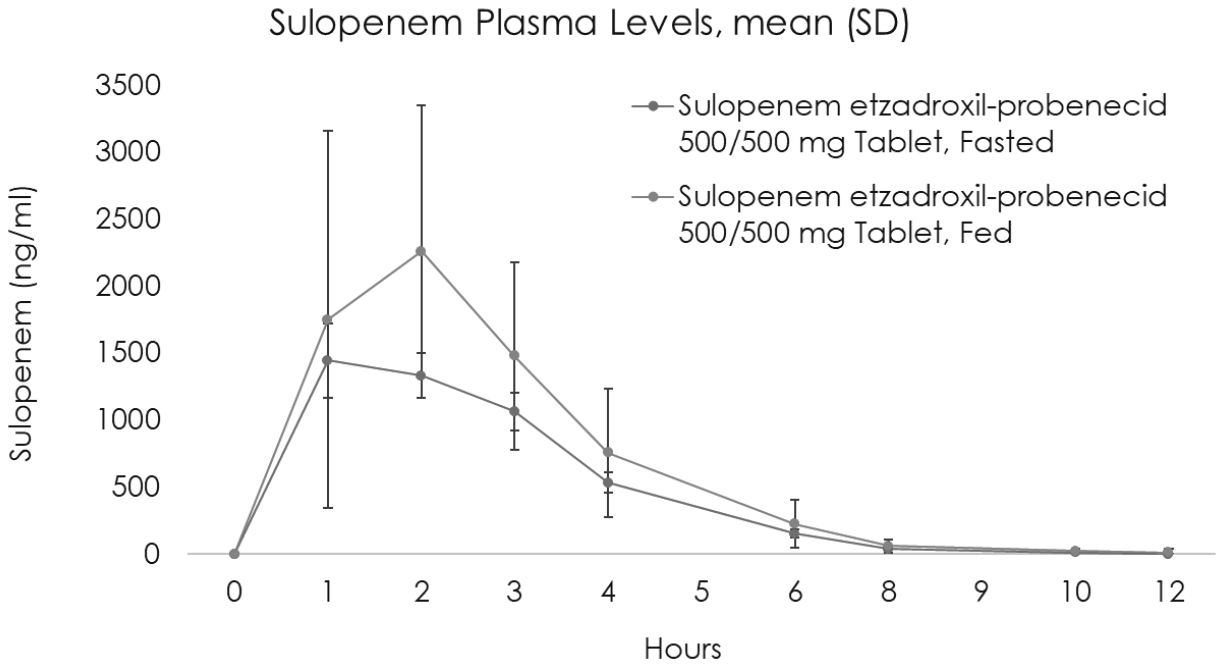
a separate tablet of probenecid demonstrated an increase in the time over MIC (of a 12 hour dosing interval) and AUC of sulopenem, as shown in the table below.

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

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

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

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



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

Sulopenem, IV Formulation

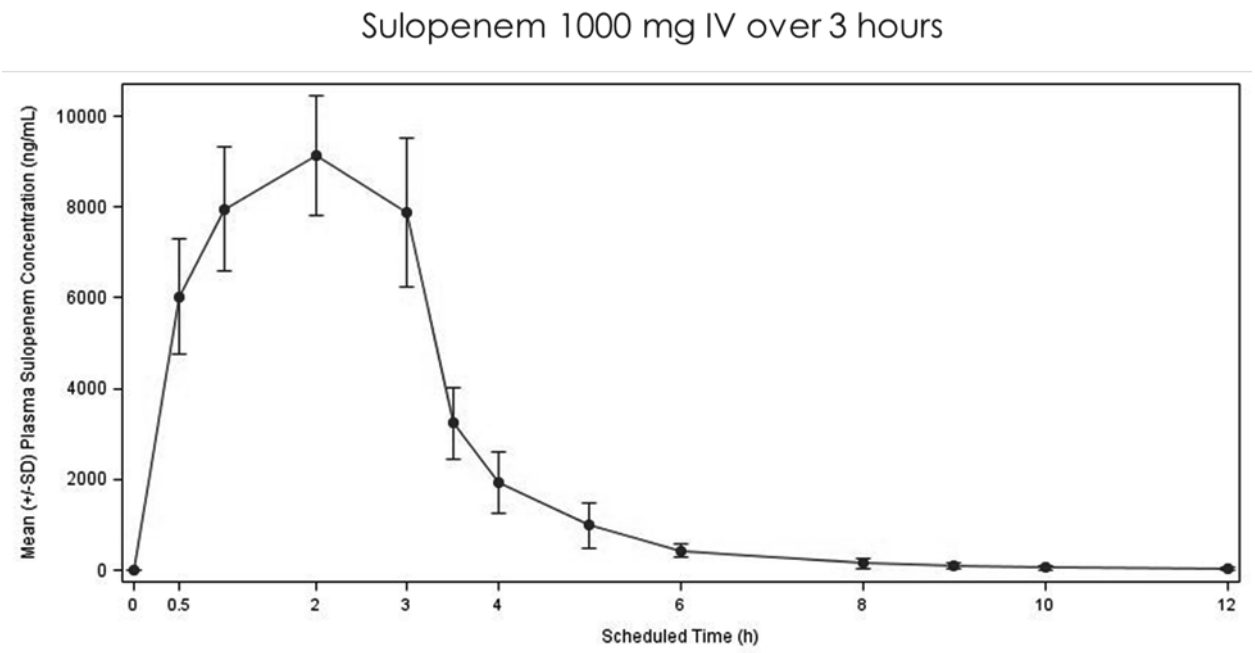
Doses of sulopenem up to 2800 mg as a single IV dose and 2000 mg BID, or twice daily, of sulopenem as IV over fourteen days were studied in three Phase 1 clinical trials in healthy adults, one study in patients with renal insufficiency in the United States and two Phase 1 clinical trials in Japan. Results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

	N	Dose (mg)	Infusion duration (h)	C_{max} (µg/mL)	$AUC_{0-¥}$ (µg hr/mL)	$T_{1/2}$ (h)	CL_{total} (mL/min/kg)
Day 1	8	800	3	7.27	22.4	0.83	
	8	1200	1	32.5	42.3	1.04	
	8	1200	2.5	16.6	41.9	1.12	
Day 14	5	800	3	8.97	26.5	0.89	15.4
	6	1200	1	30.7	41.4	1.05	14.7
	6	1200	2.5	13.5	34.6	1.01	18.8

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

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

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



Modeling and Dose Selection

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

Japanese Clinical Data

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Phase 2 Clinical Trial with sulopenem and sulopenem etzadroxil

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

Phase 3 Clinical Trials

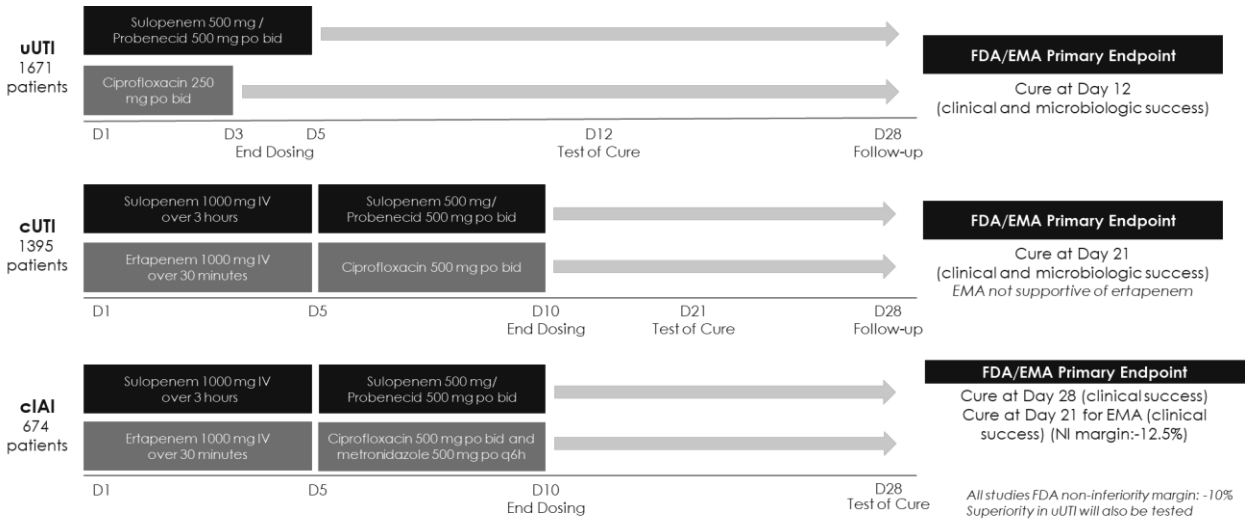
Based on FDA Guidance from February 2015 (Complicated Intra-Abdominal Infections: Developing Drugs for Treatment. Guidance for Industry; Complicated Urinary Tract Infections: Developing Drugs for Treatment. Guidance for Industry) and on recently conducted studies by other sponsors, we negotiated SPA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

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

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

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

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



Safety Profile of Oral Sulopenem and Sulopenem

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

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

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

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

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

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

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

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

Pfizer License Agreement

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

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

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

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

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

Intellectual Property

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

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

Intellectual Property Relating to Oral Sulopenem

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

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

Patent Term and Patent Term Extensions

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

Trade Secrets

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

Competition

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

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

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

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

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

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

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

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

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

Government Regulation and Product Approval

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

United States Government Regulation

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

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

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

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

Preclinical Studies

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

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

Clinical Trials

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

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

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

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

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

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

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

Expanded Access to an Investigational Drug for Treatment Use

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

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

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

Marketing Approval

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

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

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

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

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

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

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

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

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

Special FDA Expedited Review and Approval Programs

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

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

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

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

Post-Approval Requirements

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

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

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

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

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

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

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

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

Exclusivity and Approval of Competing Products

Hatch-Waxman Exclusivity

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

Qualified Infectious Disease Product Exclusivity

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

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

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

Pediatric Exclusivity

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

Regulation Outside of the United States

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

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

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

Brexit and the Regulatory Framework in the United Kingdom

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

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

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

General Data Protection Regulation

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

Pharmaceutical Coverage and Reimbursement

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

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

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

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

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

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

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

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

Other Healthcare Laws

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

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

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

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

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

Healthcare Reform

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

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

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

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

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

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

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

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

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

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

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

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

Commercialization Strategy and Organization

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

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

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

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

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

Manufacturing

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

Employees

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

Our Corporate Information

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

Available Information

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

Item 1A. Risk Factors.

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

Risks Related to Our Financial Position and Capital Requirements

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Clinical Development and Commercialization

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

process that may require the provision of supporting scientific, clinical and cost effectiveness data for the use 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. As this rule has only recently been implemented, we cannot at present assess its potential impact on sulopenem.

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Dependence on Third Parties

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Intellectual Property

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Regulatory Approval and Other Legal Compliance Matters

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to replace elements of the ACA during the next Congressional session.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Employee Matters and Managing Growth

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Taxation

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Ordinary Shares

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

our being obligated to issue to Sarissa ordinary shares representing 30% or more of our issued voting share capital. While we intend to seek a waiver from the Irish Takeover Panel of any resulting obligation of Sarissa to make a general offer as a result of exchange of these Exchangeable Notes, we cannot be certain that we will be able to obtain such a waiver, and we expect that such a waiver would be conditioned upon the passing of a resolution, on a poll, by our independent shareholders to approve a maximum potential issuance to Sarissa of up to 60% of our ordinary shares as a result of the exchange of these Exchangeable Notes.

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

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

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

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

We could be subject to securities class action litigation.

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

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

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

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

Item 3. Legal Proceedings.

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

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

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

Holders of Record

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

Dividends

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

Recent Sales of Unregistered Securities

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

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

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

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

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

Use of Proceeds from Registered Securities

Not applicable.

Purchases of Equity Securities by the Issuer

None.

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

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

Overview

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

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

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

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

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

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

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

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

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

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

Components of Our Results of Operations

Revenue

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

Operating Expenses

Research and Development Expenses

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

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

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

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

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

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

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

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

General and Administrative Expenses

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

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

Interest (Expense) Income, Net

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

Other Income, Net

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

Provision for Income Taxes

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

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

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

Critical Accounting Policies and Significant Judgments and Estimates

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

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

Accrued Research and Development Expenses

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

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

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

Share-Based Compensation

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

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

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

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

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

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

We have elected to account for forfeitures as they occur.

Determination of the Fair Value of Ordinary Shares prior to IPO

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

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

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

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

Results of Operations

Comparison of the Years Ended December 31, 2019 and 2018

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

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

Revenue

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

Research and Development Expenses

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

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

General and Administrative Expenses

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

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

Comparison of the Years Ended December 31, 2018 and 2017

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

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

Revenue

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

Research and Development Expenses

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

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

General and Administrative Expenses

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

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

Liquidity and Capital Resources

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

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

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

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

Secured credit facility

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

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

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

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

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

Cash Flows

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

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

Operating Activities

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

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

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

Investing Activities

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

Financing Activities

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

Funding Requirements

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

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

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

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

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

Contractual Obligations and Commitments

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

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

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

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

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

Emerging Growth Company Status

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

Off-Balance Sheet Arrangements

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

Recently Issued Accounting Pronouncements

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

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

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

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

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

Item 8. Financial Statements and Supplementary Data.

ITERUM THERAPEUTICS PLC

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

Going Concern

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

Change in Accounting Principle

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

Basis for Opinion

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

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

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

/s/ KPMG

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

Dublin, Ireland
March 12, 2020

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

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

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

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

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

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

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

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

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

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

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

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

(1) Nature of Operations and Basis of Presentation

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

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

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

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

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

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

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

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

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

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

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

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

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

(2) Summary of Significant Accounting Policies

Use of Estimates

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

Comprehensive Loss

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

Consolidation

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

Short-term Investments

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

Cash and Cash Equivalents

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

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

Foreign Currencies

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

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

Property and Equipment

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

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

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

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

Leases

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

Research and Development Expenses

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

Accrued Research and Development Expenses

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

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

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

Patent Costs

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

Share-Based Compensation

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

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

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

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

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

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

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

Grant Awards

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

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

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

Research and Development Credits

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

Fair Value of Financial Instruments

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

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

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

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

Borrowings

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

Concentration of Credit Risk

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

Income Taxes

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

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

(In thousands, except share and per share data)

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

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

Net Loss Per Ordinary Share

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

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

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

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

Segment and Other Information

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

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

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

(In thousands, except share and per share data)

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

Long lived assets	December 31, 2019	December 31, 2018
Ireland	$ 10,936	$ 4,565
U.S.	3,037	245
Total	$ 13,973	$ 4,810

Retirement Plan

The Company has a defined contribution plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all U.S. employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pre-tax basis. If the 401(k) Plan is considered top-heavy at the end of the financial year, with key employee accounts accounting for >60% of total 401(k) Plan assets, the Company is required to contribute a deferral rate of up to 3% to the 401(k) Plan on behalf of certain employees. The Company was not required to make a top-heavy contribution for the year ended December 31, 2019. The Company made contributions of $114 and $33 for the years ended December 31, 2018 and 2017, respectively.

Inventory

Inventories are valued at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method for all inventories. The Company's policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. The estimate of excess quantities is subjective and primarily dependent on the estimates of future demand for a particular product. If the estimate of future demand changes, the Company considers the impact on the reserve for excess inventory and adjusts the reserve as required. Increases in the reserve are recorded as charges in cost of product sales. For product candidates that have not been approved by the FDA, inventory used in clinical trials is expensed at the time of production and recorded as research and development expenses. For products that have been approved by the FDA, inventory used in clinical trials is expensed at the time the inventory is packaged for the clinical trial. Prior to an advisory committee providing a recommendation to the FDA that the Company's application should be approved, costs related to manufacturing the product candidates are recorded as research and development expenses. All direct manufacturing costs incurred after this recommendation will be capitalized into inventory. The Company had no inventory as of December 31, 2019 or December 31, 2018.

Contingent Consideration

Certain license agreements contain milestone payments that could result in the requirement to make contingent consideration payments, see Note 12 for further details. Contingent consideration is recorded at the acquisition date estimated fair value of the contingent payment. The fair value of the contingent consideration is measured at each reporting period. Any related unwinding of discount is recognized as a finance expense. Other changes in fair value are recognized in profit or loss or capitalized as an intangible asset depending on the stage of development. As of December 31, 2019, no milestones had been met that required the Company to recognize contingent consideration.

Recently Adopted Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board (FASB) issued ASU 2016-02, *Leases* (Topic 842) in order to increase transparency and comparability among organizations by recognizing lease assets and lease liabilities on the balance sheet for those leases classified as operating leases under prior GAAP. In July 2018, the FASB issued ASU 2018-11 *Leases* (Topic 842): *Targeted Improvements* which provides the option to adopt the standard retrospectively for each prior period presented, as initially set out in ASU 2016-02, or as of the adoption date with a cumulative-effect adjustment to the opening balance of retained earnings. In March 2019, the FASB issued ASU 2019-03 *Leases* (Topic 842): *Codification Improvements* amending the transition disclosures for Topic 842, in that all companies are exempt from certain interim period transition disclosure requirements.

ASU 2016-02 requires a lessee to recognize a liability to make lease payments (the lease liability) and a right-of-use asset, representing its right to use the underlying asset for the lease term, on the balance sheet. The Company adopted ASU 2016-02 in the first quarter of 2019 utilizing the modified retrospective transition method with an effective date as the date of initial application.

(In thousands, except share and per share data)

Consequently, prior period balances and disclosures have not been restated. The adoption of ASU 2016-02 on January 1, 2019 resulted in the recognition of right-of-use assets of $7.6 million and operating lease liabilities of $7.8 million, however, the adoption of the standard did not have an impact on the Company's beginning retained earnings, results from operations or cash flows. See Note 7 for further information regarding the impact of the adoption of ASU 2016-02 on the Company's consolidated financial statements.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share* (Topic 260), *Distinguishing Liabilities from Equity* (Topic 480), *Derivatives and Hedging* (Topic 815), I. Accounting for Certain Financial Instruments with Down Round Features, II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception.

Part I applies to entities that issue financial instruments such as warrants, convertible debt or convertible preferred shares that contain down-round features. Part II replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. ASU 2017-11 is required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. The adoption of ASU 2017-11 did not have an impact on the Company's consolidated financial statements.

In June 2018, the FASB issued *ASU 2018-07, Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting*.

ASU 2018-07 expands the scope of Topic 718 to include all share-based payment transactions for acquiring goods and services from nonemployees. ASU 2018-07 specifies that Topic 718 applies to all share-based payment transactions in which the grantor acquires goods and services to be used or consumed in its own operations by issuing share-based payment awards. ASU 2018-07 also clarifies that Topic 718 does not apply to share-based payments used to effectively provide (1) financing to the issuer or (2) awards granted in conjunction with selling goods or services to customers as part of a contract accounted for under ASC 606. ASU 2018-07 is required to be adopted for annual periods beginning after December 15, 2019, including interim periods within those fiscal years. The adoption of ASU 2018-07 did not have an impact on the Company's consolidated financial statements.

Recent Accounting Pronouncements

There are no recently issued accounting pronouncements that will have a material impact on the Company's consolidated financial statements and related disclosures.

(3) Fair Value of Financial Assets and Liabilities

The following table presents information about the Company's financial assets that were carried at fair value on a recurring basis on the consolidated balance sheet as of December 31, 2019 and December 31, 2018 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value.

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

December 31, 2018 Assets	Total	Level 1	Level 2	Level 3
Short-term investments	$ 40,000	40,000	—	—
Other assets – advance payment to supplier	2,649	—	—	2,649
Total	$ 42,649	40,000	—	2,649

See Note 4 for further details on short-term investments. The other asset above relates to advance payments made to a supplier that were recorded at fair value using the discounted cash flow model, or DCF, as of December 31, 2019 and December 31, 2018. The fair value measurements of these advance payments were determined based on significant unobservable inputs, including a discount rate of 15% and the expected time to recovery of the payment. Changes to the inputs described above are not expected to have a material impact on the company's financial position and results of operations in any given period. See Note 12 — Payments to Supplier, for further details on these advance payments.

(In thousands, except share and per share data)

The following table presents information about the Company's long-term debt which was carried at amortized cost on the consolidated balance sheet as of December 31, 2019 and December 31, 2018 and indicates the fair value hierarchy of the valuation inputs utilized to determine the approximate fair value.

December 31, 2019

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

December 31, 2018

Liabilities	Book Value	Approximate Fair Value	Level 1	Level 2	Level 3
Current portion of long-term debt	$ 1,019	$ 1,019	—	1,019	—
Long-term debt, less current portion	13,079	13,035	—	13,035	—
Total	$ 14,098	$ 14,054	—	14,054	—

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

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

There have been no transfers of assets or liabilities between the fair value measurement levels.

(4) Short-term Investments

The Company classifies its short-term investments as available for sale. Short-term investments comprise highly liquid investments with minimum "A-" rated securities. Investments are reported at fair value with unrealized gains or losses recorded in the consolidated statements of operations and comprehensive loss. Any differences between the cost and fair value of investments are represented by unrealized gains or losses. The fair values of short-term investments are represented by Level 1 fair value measurements – quoted prices in active markets for identical assets.

The Company did not hold any short-term investments as of December 31, 2019. The following table represents the Company's available for sale short-term investments by major security type as of December 31, 2018:

December 31, 2018

Available for sale	Cost Total	Unrealized gains	Unrealized (losses)	Fair Value Total	Maturity by period: Less than 1 year	Maturity by period: 1 to 5 years
Commercial paper	$ 35,745	272	(9)	36,008	36,008	—
U.S. Treasury and Agency Bonds	3,977	15	—	3,992	3,992	—
Total	$ 39,722	287	(9)	40,000	40,000	—

(In thousands, except share and per share data)

(5) Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following:

	December 31, 2019	December 31, 2018
Deferred financing expenses (1)	$ 2,339	—
Prepaid research and development expenses	1,679	5,351
Short-term deposits	1,139	959
Research and development tax credit receivable	1,036	404
Prepaid insurance	569	438
Value added tax receivable	68	159
Other prepaid assets	50	921
Interest receivable	7	158
Total	$ 6,887	$ 8,390

(1) See note 15 to the consolidated financial statements for further details deferred financing expenses.

(6) Property and Equipment, net

Property and equipment and related accumulated depreciation are as follows:

	December 31, 2019	December 31, 2018
Leasehold improvements	$ 592	$ 592
Furniture and fixtures	120	120
Laboratory equipment	81	81
Computer equipment	132	108
	925	901
Less: accumulated depreciation	(353)	(201)
	$ 572	$ 700

Depreciation expense was $152, $136 and $65 for the years ended December 31, 2019, 2018 and 2017, respectively.

(7) Leases

The Company has entered into a number of operating leases, primarily for office space and commercial property. These leases have terms which range from four to 19 years, and generally include one or more options to terminate or renew. The termination options can reduce the lease term for periods ranging from five to 10 years, however the remaining lease terms do not represent these early termination dates as management has concluded that it is reasonably certain that the Company will not exercise these options. The renewal terms can extend the lease term for additional periods ranging from three to five years. These renewal options are represented in the remaining lease term as management has concluded that it is reasonably certain that the Company will exercise the renewal option. Certain leases contain variable lease payments, including payments based on an index or rate. Variable lease payments based on an index or rate are initially measured using the index or rate in effect at lease commencement. Certain agreements contain both lease and non-lease components. The Company has elected to separately account for these components in determining the lease liabilities and right-of-use assets. The Company's lease agreements generally do not provide an implicit borrowing rate, therefore an internal incremental borrowing rate was determined based on information available at lease commencement date for the purposes of determining the present value of lease payments. The Company used the incremental borrowing rate on January 1, 2019 for all leases that commenced prior to that date. All operating lease expenses are recognized on a straight-line basis over the lease term. The Company recognized $1,015 of operating lease costs for right-of-use assets during the year ended December 31, 2019.

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

(In thousands, except share and per share data)

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

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

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

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

	December 31, 2019
Other assets	$7,144
Other current liabilities	$580
Other liabilities	6,748
Total lease liabilities	$7,328

The Company has recorded the reduction in carrying amount of the right-of-use assets and the change in the lease liability in the Other category within the operating section of the consolidated statement of cash flows.

Future lease payments included in the measurement of lease liabilities on the consolidated balance sheet as of December 31, 2019 for the following five fiscal years and thereafter were as follows:

Due in 12 month period ended December 31,	
2020	$1,099
2021	1,023
2022	1,032
2023	1,038
2024	1,042
Thereafter	5,641
	$10,875
Less imputed interest	(3,547)
Total lease liabilities	$7,328

As of December 31, 2018, future minimum lease payments, as defined under the previous lease accounting guidance of ASC Topic 840, under non-cancelable operating leases for the following five fiscal years and thereafter were as follows:

Due in 12 month period ended December 31,	
2019	$904
2020	1,020
2021	1,030
2022	985
2023	766
Thereafter	2,356
	$7,061

(In thousands, except share and per share data)

(8) Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2019	December 31, 2018
Accrued clinical trial costs	$ 9,866	$ 2,849
Accrued payroll and bonus expenses	1,207	1,804
Accrued manufacturing expenses	136	1,439
Accrued other expenses	1,249	954
Total	$ 12,458	$ 7,046

(9) Shareholders' (Deficit) / Equity

The Company's capital structure consists of ordinary shares, undesignated preferred shares and, prior to the completion of the Company's IPO on May 30, 2018, convertible preferred shares with certain rights and privileges summarized below. Under Irish law, the Company is prohibited from allotting shares without consideration. Accordingly, at least the nominal value of the shares issued underlying any restricted share award, restricted share unit, performance share award, bonus share or any other share based grant must be paid pursuant to the Irish Companies Act 2014 ("Irish Companies Act").

Ordinary Shares

The Company was initially incorporated without a cap on its authorized share capital as permitted by the Irish Companies Act. On October 14, 2015, the Company authorized and issued 413,110 ordinary shares with a par value of $0.01 per share (after taking account of the reverse share split and redenomination of the par value of the ordinary shares from $0.01571 (the nominal value resulting from the reverse share split) to $0.01 on May 15, 2018). On March 13, 2018, the Company redenominated its 44,557,606 authorized and 413,110 issued ordinary shares from $0.0001 to $0.001 per share in accordance with section 83(1)(c) of the Irish Companies Act.

On November 18, 2015, the Company increased the authorized ordinary share capital to 3,659,453 shares with a par value of $0.01 per share.

On May 18, 2017, the Company increased the authorized ordinary share capital to 7,956,715 shares with a par value of $0.01 per share.

On February 16, 2018, the Company increased its authorized ordinary shares by 36,600,891 to 44,557,606 ordinary shares with a par value of $0.01 per share.

On May 30, 2018, the Company increased its authorized ordinary shares by 5,442,394 to 50,000,000 ordinary shares of $0.01 each.

On December 14, 2018, Iterum Therapeutics plc ("ITP") and Iterum Therapeutics International Limited ("ITIL") entered into a subscription agreement with a supplier of ITIL pursuant to which the supplier agreed to subscribe for ordinary shares in ITP in satisfaction of amounts due and owing under certain commercial agreements entered into between the supplier and ITIL (the "Subscription Agreement"). Pursuant to the terms of the Subscription Agreement, upon receipt by ITIL of a valid invoice from the supplier, ITP can elect to require the supplier to subscribe for ordinary shares in the capital of ITP (up to a maximum of 700,000 ordinary shares in total) to the value of the invoiced amount (a "Subscription"). On a Subscription, the supplier will direct ITIL to pay ITP such invoiced amount as subscription monies on the supplier's behalf in satisfaction of the invoiced amount.

On December 14, 2018, ITP elected that the supplier subscribe for 190,615 ordinary shares for an aggregate subscription price of $1.36 million (the "December Subscription Monies") upon receipt by ITIL of valid invoices up to that amount from the supplier (the "Invoiced Amount"). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $1.36 million (€1.20 million) to ITP in satisfaction of the supplier's obligation to pay the December Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

On July 15, 2019, ITP elected that the supplier subscribe for 17,222 ordinary shares for an aggregate subscription price of $0.11 million (the "July Subscription Monies") upon receipt by ITIL of valid invoices up to that amount from the supplier (the "Invoiced Amount"). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $0.11 million (€0.10 million) to ITP in satisfaction of the supplier's obligation to pay the July Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

On August 19, 2019, ITP elected that the supplier subscribe for 245,493 ordinary shares for an aggregate subscription price of $1.67 million (the "August Subscription Monies") upon receipt by ITIL of valid invoices up to that amount from the supplier (the "Invoiced Amount"). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $1.67 million (€1.50 million) to ITP in satisfaction of the supplier's obligation to pay the August Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

On September 30, 2019, ITP elected that the supplier subscribe for 199,056 ordinary shares for an aggregate subscription price of $1.26 million (the "September Subscription Monies") upon receipt by ITIL of valid invoices up to that amount from the supplier (the "Invoiced Amount"). On that date, ITP, ITIL and the supplier executed a payment direction letter pursuant to which the parties directed ITIL to pay $1.26 million (€1.15 million) to ITP in satisfaction of the supplier's obligation to pay the September Subscription Monies to ITP and ITIL's obligation to pay the invoiced amount to the supplier.

The holders of ordinary shares are entitled to one vote for each share held. The holders of ordinary shares have no preemptive or other subscription rights, and there are no redemption or sinking fund provisions with respect to such shares.

Undesignated Preferred Shares

On May 30, 2018, the Company created a new class of undesignated preferred shares of $0.01 each, 100,000,000 of which were authorized immediately prior to closing of the initial public offering. The Directors are authorized by the Company's Articles of Association to determine the rights attaching to the undesignated preferred shares including rights of redemption, rights as to dividends, rights on winding up and conversion rights. There were no undesignated preferred shares in issue as of December 31, 2019 or December 31, 2018.

Convertible Preferred Shares

On November 18, 2015, the Company authorized 3,022,915 Series A convertible preferred shares with a par value of $0.01 per share. On the same day, the Company issued 1,514,320 Series A convertible preferred shares for a purchase price of $15.71 per share for: (1) gross cash proceeds of $20,701; (2) the issue of 190,961 convertible preferred shares to Pfizer as part consideration for the license agreement; and (3) the conversion of $90 debt owed by the Company to its founders for a total of 5,728 preferred shares (after taking account of the reverse share split and redenomination of the par value of the convertible preferred shares from $0.01571 (the nominal value resulting from the reverse share split) per share to $0.01 on May 15, 2018). On March 13, 2018, the Company redenominated its 3,032,463 authorized and 3,032,457 issued Series A convertible preferred shares from $0.0001 to $0.001 par value per share in accordance with section 83(1)(c) of the Irish Companies Act.

On December 9, 2016, the Company authorized 9,548 Series A convertible preferred shares with a par value of $0.01 per share.

On December 16, 2016, the Company issued 1,518,137 Series A convertible preferred shares for a purchase price of $15.71 per share for: (1) gross cash proceeds of $20,851; and (2) the issue of an additional 190,961 convertible preferred shares to Pfizer as part consideration for the license agreement.

On May 18, 2017, the Company authorized 2,654,215 Series B-1 convertible preferred shares with a par value of $0.01 per share and 1,042,728 Series B-2 convertible preferred shares with a par value of $0.01 per share (the "Series B convertible preferred shares"). On the same day, the Company issued 2,654,206 Series B-1 convertible preferred shares for a purchase price of $17.28 per share, for gross cash proceeds of $45,867 (after taking account of the reverse share split and redenomination of the par value of the convertible preferred shares from $0.01571 (the nominal value resulting from the reverse share split) per share to $0.01 on May 15, 2018). On March 13, 2018, the Company redenominated its 4,801,493 authorized and 4,363,856 issued Series B convertible preferred shares from $0.0001 to $0.001 par value per share in accordance with section 83(1)(c) of the Irish Companies Act.

On February 16, 2018, the Company increased its authorized Series B-2 convertible preferred shares to 2,147,278 shares with a par value of $0.01 per share. On the same day, the Company issued 1,709,650 Series B-2 convertible preferred shares for consideration of $18.85 per share, for gross cash proceeds of $32,230.

On May 30, 2018, immediately prior to the completion of the Company's IPO, holders of convertible preferred shares of Iterum Therapeutics Plc exchanged their preferred shares for ordinary shares of Iterum Therapeutics Plc on a one-for-one basis and all convertible preferred shares were subsequently cancelled.

Prior to the exchange and cancellation of preferred convertible shares on May 30, 2018, the ordinary shares were subordinate to the convertible preferred shares with respect to dividend rights and rights upon liquidation, winding up and dissolution of the Company and the holders of ordinary shares were entitled to liquidation proceeds after all liquidation preferences for the convertible preferred shares were satisfied.

(10) Share-Based Compensation

On November 18, 2015, the Company's Board of Directors adopted and approved the 2015 Equity Incentive Plan (the "2015 Plan"), which authorized the Company to grant up to 223,424 ordinary shares in the form of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units and other share awards. The types of share-based awards, including the rights amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors. The purpose of the 2015 Plan is to provide the Company with the flexibility to issue share-based awards as part of an overall compensation package to attract and retain qualified personnel. On May 18, 2017, the Company amended the 2015 Plan to increase the number of ordinary shares available for issuance under the 2015 Plan by 219,605 shares to 443,029 shares.

On March 14, 2018, the Company's Board of Directors adopted and approved the 2018 Equity Incentive Plan (the "2018 Plan"), which became effective upon the execution and delivery of the underwriting agreement related to the Company's IPO. No further grants will be made under the 2015 Plan. The ordinary shares underlying any options that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2015 Plan will not be added back to the ordinary shares available for issuance.

The 2018 Plan authorizes the Company to grant up to 1,018,459 ordinary shares in the form of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share units, performance share awards, performance cash awards and other share awards. The types of share-based awards, including the amount, terms, and exercisability provisions of grants are determined by the Company's Board of Directors. The ordinary shares underlying any options that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2018 Plan will be added back to the ordinary shares available for issuance under the 2018 Plan.

On December 5, 2018, pursuant to powers delegated to it by the Board of Directors of the Company, the Compensation Committee approved an increase in the number of ordinary shares available to be granted pursuant to the 2018 plan by 4% of the total number of shares of the Company's issued share capital on December 31, 2018, being 574,081 ordinary shares.

Restricted Ordinary Shares

In connection with the Company's formation, 413,110 restricted ordinary shares were issued on October 14, 2015 to the Company's founders at par value. These ordinary shares are subject to various restrictions pursuant to ordinary share purchase agreements between the Company and each founder, including restrictions on transfer and a Company right of repurchase. The restricted ordinary shares were 25% vested as of October 14, 2016 and 1/36th of the remaining restricted ordinary shares vested on a monthly basis thereafter (subject to acceleration of vesting in connection with certain change of control transactions). A change in status occurred on November 18, 2015 when the founders became employees of the Company. The grant date of these shares is now considered to be November 18, 2015 when the fair value was $3.14 per share.

The Company records share-based compensation expense for the restricted ordinary shares based on the grant date fair value. The Company recorded an expense of $260, $332 and $333 for the years ended December 31, 2019, 2018 and 2017, respectively. There was no unamortized compensation expense related to restricted ordinary shares as of December 31, 2019. Total unamortized compensation expense related to restricted ordinary shares was $260 and $592 as of December 31, 2018 and December 31, 2017, respectively, and was recognized over a weighted average period of 0.79 years and 1.79 years.

(In thousands, except share and per share data)

A summary of the Company's restricted ordinary share activity and related information is as follows:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested at December 31, 2016	292,620	$ 3.14
Granted	—	
Vested	(103,278)	$ 3.14
Forfeited	—	
Unvested at December 31, 2017	189,342	$ 3.14
Granted	—	
Vested	(103,274)	$ 3.14
Forfeited	—	
Unvested at December 31, 2018	86,068	$ 3.14
Granted	—	
Vested	(86,068)	$ 3.14
Forfeited	—	
Unvested at December 31, 2019	—	$ 3.14

Share Options

Unless specified otherwise in an individual option agreement, share options granted under the 2015 Plan and the 2018 Plan generally have a ten year term and a four year vesting period. The vesting requirement is conditioned upon a grantee's continued service with the Company during the vesting period. Once vested, all awards are exercisable from the date of grant until they expire. The option grants are non-transferable. Vested options generally remain exercisable for 90 days subsequent to the termination of the option holder's service with the Company. In the event of an option holder's disability or death while employed by or providing service to the Company, the exercisable period extends to twelve months or eighteen months, respectively.

The fair value of options granted during the years ended December 31, 2019, 2018 and 2017 was estimated using the Black-Scholes option-pricing model. The inputs for the Black-Scholes model require management's significant assumptions. The risk-free interest rate was based on a normalized estimate of the 7-year U.S. treasury yield. The Company has estimated the expected term utilizing the "simplified" method for awards that qualify as "plain vanilla". The Company does not have sufficient company-specific historical and implied volatility information and it therefore estimates its expected share volatility based on historical volatility information of reasonably comparable guideline public companies and itself. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price. Expected dividend yield is based on the fact that the Company has never paid cash dividends, its ability to pay cash dividends is currently prohibited by the terms of its credit facility with SVB and the Company's future ability to pay cash dividends on its shares may be limited by the terms of any future debt or preferred securities. The Company has elected to account for forfeitures as they occur.

The Company granted 512,778, 479,986 and 198,798 share options to employees and directors during the years ended December 31, 2019, 2018 and 2017, respectively. There were 837,386, 566,813 and 228,809 unvested employee and director options outstanding as of December 31, 2019, December 31, 2018 and December 31, 2017, respectively. Total expense recognized related to the employee and director share options was $1,388, $669 and $59 for the years ended December 31, 2019, 2018 and 2017, respectively. Total unamortized compensation expense related to employee and director share options was $3,342, $2,822 and $396 as of December 31, 2019, December 31, 2018 and December 31, 2017, respectively, expected to be recognized over a remaining weighted average vesting period of 2.61 years, 3.07 years and 3.51 years as of December 31, 2019, December 31, 2018 and December 31, 2017, respectively.

The range of assumptions that the Company used to determine the grant date fair value of employee and director options granted were as follows:

	Year ended December 31,		
	2019	2018	2017
Volatility	68.9 - 74.5%	60%	60%
Expected term in years	5.50 - 6.25	6.25	6.25
Dividend rate	0%	0%	0%
Risk-free interest rate	1.73 - 2.57%	2.16 - 2.91%	1.63%
Share price	3.55 - 6.80	7.06 - 13.00	3.30 - 4.40
Fair value of option on grant date	2.37 - 4.41	4.41 - 7.49	1.88 - 2.50

The following table summarizes the number of options outstanding and the weighted-average exercise price:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value (in thousands)
Options outstanding December 31, 2016	49,330	$ 3.14	8.51	
Granted	198,798	$ 3.36		
Options outstanding December 31, 2017	248,128	$ 3.31	9.44	
Granted	479,986	$ 12.60		
Exercised	(2,008)	$ 3.30		
Forfeited	(60,887)	$ 10.99		
Options outstanding December 31, 2018	665,219	$ 9.31	8.93	395
Granted	512,778	$ 5.94		
Exercised	(18,232)	$ 3.29		
Forfeited	(8,726)	$ 7.43		
Expired	(769)	$ 6.77		
Options outstanding December 31, 2019	1,150,270	$ 7.92	8.59	254
Exercisable at December 31, 2019	312,884	$ 8.82	8.02	157

The aggregate intrinsic value of share options is calculated as the difference between the exercise price of the share options and the fair value of the Company's ordinary shares for those share options that had exercise prices lower than the fair value of the Company's ordinary shares as of December 31, 2019 and December 31, 2018.

The weighted average grant-date fair value per share of share options granted during the years ended December 31, 2019, 2018 and 2017 was $3.80, $7.25 and $1.91, respectively.

Restricted Share Units (RSUs)

The Company granted 31,367 and 36,924 RSUs to directors during the years ended December 31, 2019 and 2018, respectively. No RSUs were granted prior to the year ended December 31, 2018.

(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

The fair value of the RSUs is determined on the date of grant based on the market price of the Company's ordinary shares on that date. The fair value of RSUs is expensed ratably over the vesting period, which is generally one year for directors. Total expense recognized related to the RSUs was $313 and $289 for the years ended December 31, 2019 and 2018, respectively. Total unamortized compensation expenses related to the RSUs was $99 and $191 as of December 31, 2019 and December 31, 2018, respectively, expected to be recognized over a remaining average vesting period of 0.45 years and 0.40 years as of December 31, 2019 and December 31, 2018, respectively.

The Company awarded 50,000 RSUs to certain employees during the year ended December 31, 2019 which are subject to certain vesting conditions (Performance RSUs). No Performance RSUs were awarded prior to the year ended December 31, 2019.

The table below shows the number of Performance RSUs granted covering an equal number of the Company's ordinary shares and the weighted-average grant date fair value of the Performance RSUs granted:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Performance RSUs outstanding December 31, 2018	—	
Granted	50,000	$8.21
Shares vested	—	
Forfeited	—	
Performance RSUs outstanding December 31, 2019	50,000	$8.21

The weighted average grant date fair value of Performance RSUs with a market condition was determined using the Monte Carlo simulation model. The fair value of Performance RSUs is expensed ratably over the vesting period. Total expense recognized related to the Performance RSUs was $212 for the year ended December 31, 2019. Total unamortized compensation expenses related to Performance RSUs was $198 as of December 31, 2019 expected to be recognized over a remaining average vesting period of 0.81 years as of December 31, 2019.

The Company's share-based compensation expense was classified in the consolidated statements of operations and comprehensive loss as follows:

	Year ended December 31,		
	2019	2018	2017
Research and development expense	$ 723	$ 398	$ 139
General and administrative expense	1,450	892	253

(In thousands, except share and per share data)

There was a total of $3,639, $3,273 and $988 unamortized share-based compensation expense for restricted ordinary shares, options, restricted share units and performance restricted share units as of December 31, 2019, December 31, 2018 and December 31, 2017, respectively, expected to be recognized over a remaining average vesting period of 2.44 years, 2.71 years and 2.53 years as of December 31, 2019, December 31, 2018 and December 31, 2017, respectively.

(11) Income Taxes

During the years ended December 31, 2019, 2018 and 2017, the Company recorded no income tax benefits for the net operating losses incurred in each year due to its uncertainty of realizing a benefit from those items.

The provision for income taxes consists of the following components:

	Year ended December 31,		
	2019	2018	2017
Current			
U.S.	$ 444	$ 472	$ 444
Ireland	—	—	—
Total Current	$ 444	$ 472	$ 444
Deferred			
U.S.	$ —	$ —	$ —
Ireland	—	—	—
Total Deferred	$ —	$ —	$ —
Income Tax Provision	$ 444	$ 472	$ 444

Income taxes have been based on the following components of income (loss) before provision for income taxes:

	Year ended December 31,		
	2019	2018	2017
U.S.	$484	$532	$875
Ireland	(103,170)	(77,116)	(29,837)
Total	$(102,686)	$(76,584)	$(28,962)

The Irish federal statutory rate is reconciled to the effective tax rate as follows:

	Year ended December 31, 2019		Year ended December 31, 2018		Year ended December 31, 2017	
Statutory rate	12.50%	$(12,836)	12.50%	$(9,573)	12.50%	$(3,620)
Impact of U.S. tax rate	(0.07)%	72	(0.11)%	81	(0.80)%	232
Impact of valuation allowance	(12.91)%	13,258	(11.42)%	8,749	(13.64)%	3,949
Research and development tax credit	0.23%	(232)	0.45%	(341)	0.76%	(220)
Adjustments for current tax of prior periods	(0.24)%	241	0.00%	—	0.00%	—
Other, net	0.06%	(59)	(2.03)%	1,557	(0.36)%	103
Effective tax rate	(0.43)%	$444	(0.61)%	$472	(1.54)%	$444

(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,		
	2019	2018	2017
Deferred tax assets			
Share-based compensation	$ 679	$ 27	$ 3
Depreciation	(24)	(49)	6
Net operating loss carryforwards	26,195	13,648	5,409
163(j) interest expense limitation	730	115	—
Other	84	665	239
Valuation allowance	(27,664)	(14,406)	(5,657)
Total deferred tax assets	$ —	$ —	$ —
Deferred tax liabilities			
	—	—	—
Total deferred tax assets	$ —	$ —	$ —
Net deferred tax asset	$ —	$ —	$ —

As a Company incorporated in Ireland, it is principally subject to taxation in Ireland.

The Company has net operating loss carryforwards in Ireland of approximately $26,195, $13,648 and $5,409 as of the years ended December 31, 2019, 2018 and 2017, respectively, for which a full valuation allowance has been recognized as it was determined that it is more-likely-than-not that these net deferred tax assets will not be realized. The net operating loss carryforwards do not expire, but are carried forward indefinitely. Realization of these deferred tax assets is dependent on the generation of sufficient taxable income. If the Company demonstrates consistent profitability in the future, the evaluation of the recoverability of these deferred tax assets may change and the remaining valuation allowance may be released in part or in whole. While management expects to realize the deferred tax assets, net of valuation allowances, changes in estimates of future taxable income or in tax laws may alter this expectation.

On December 22, 2017, the United States federal government enacted the Tax Act, marking a change from a worldwide tax system to a modified territorial tax system in the United States. As part of this change, the Tax Act, among other changes, provided a reduction of the U.S. federal corporate income tax rate from 34% to 21%, an indefinite carryforward of net operating losses incurred in 2018 and future periods, and an interest limitation starting in 2018 with an indefinite carryforward. Any impact to the Company related to these items were accounted for in the 2017, 2018 and 2019 tax provisions with minimal impact.

A reconciliation of the beginning and ending amount of gross unrecognized tax benefits is as follows:

	2019	2018
Balance at January 1	$ 428	$ 30
Additions	2,033	398
Balance at December 31	$ 2,461	$ 428

The Company is generally subject to examination in the Company's primary tax jurisdictions for tax years beginning 2015. The Company is not currently subject to any audits or examination.

(12) Commitments and Contingencies

License Agreement

On November 18, 2015, the Company entered into a license agreement with Pfizer for the worldwide exclusive rights to research, develop, manufacture and commercialize sulopenem.

As part of the license agreement, the Company is obligated to pay Pfizer potential future regulatory milestone payments, as well as sales milestones upon achievement of net sales ranging from $250.0 million to $1.0 billion for each product type. The Company is

also obligated to pay Pfizer royalties ranging from a single-digit to mid-teens percentage based on marginal net sales of each licensed product.

Payments to Supplier

In June 2016, the Company entered into an agreement with a supplier whereby the Company would pay $2,807 (€2,500) to the supplier to acquire equipment which will be used solely to manufacture product for the Company. In June 2018, the Company entered into a supplemental agreement with this supplier whereby the Company would pay an additional $2,301 (€2,050) under the same terms as the original agreement. These payments will be offset against the price of the product to be supplied under a future supply agreement. No balance remained outstanding to the supplier as of December 31, 2019. $1,604 remained outstanding to the supplier as of December 31, 2018.

Contingencies

Liabilities for loss contingencies arising from claims, assessments, litigation, fines, penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. At each reporting date the Company evaluates whether or not a potential loss amount or a potential loss range is probable and reasonably estimable under the provisions of the authoritative guidelines that address accounting for contingencies. The Company expenses costs as incurred in relation to such legal proceedings. The Company is not currently involved in any legal matters arising in the normal course of business.

Under the terms of their respective employment agreements, each of the executive officers is eligible to receive severance payments and benefits upon a termination without "cause" or due to "permanent disability", or upon "resignation for good reason", contingent upon the named executive officer's continued performance for the Company.

(13) Debt

On April 27, 2018, the Company's subsidiaries, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited and Iterum Therapeutics US Limited (The Borrowers), entered into a Loan and Security Agreement with SVB pursuant to which SVB agreed to lend the Borrowers up to $30,000 in two term loans. $15,000 of the secured credit facility was funded on closing. A second draw of up to $15,000 was available to the Company through October 31, 2019, upon satisfaction of either of the following: (i) the achievement by the Company of both non-inferiority and superiority primary endpoints from its Phase 3 uncomplicated urinary tract infection (uUTI) trial, as well as reporting satisfactory safety data from the trial, or (ii) the achievement of non-inferiority primary endpoints from both its Phase 3 uUTI and complicated urinary tract infection (cUTI) trials, as well as reporting satisfactory safety data from the trials. A non-utilization fee of 1.50% of the aggregate undrawn principal amount was to apply if the Company satisfied the above conditions but chose not to draw down the second term loan. The Company did not satisfy the conditions for the second draw above before the deadline of October 31, 2019.

Required monthly amortization payments for the initial $15,000 draw commenced on November 1, 2019 and total principal repayments of $1,034 were made during the year ended December 31, 2019. Interest accrues at a floating per annum rate equal to the greater of (i) 8.31%; or (ii) 3.89% above the Wall Street Journal prime rate, and is payable monthly in arrears. All outstanding principal, plus a 4.20% final interest payment, will be due and payable on the earliest to occur of March 1, 2022 (the maturity date), the acceleration of the term loan or the prepayment of the term loan. The final payment fee of $630 which represents 4.2% of the funded loan, is accreted using the effective interest method over the life of the loan as interest expense. Voluntary prepayments are permitted at any time, subject to a prepayment fee of 4.00% in the first year, 3.00% in the second year, and 2.00% thereafter.

In connection with the initial $15,000 draw, the Company issued SVB and Life Sciences Fund II LLC (LSF) warrants to purchase an aggregate of 19,890 Series B convertible preferred shares (which converted into warrants to purchase 19,890 ordinary shares upon the Company's IPO) at an exercise price of $18.85 per share. Had the second term loan been drawn down, each of SVB and LSF would have been automatically entitled to purchase additional ordinary shares in an aggregate amount equal to 2.50% of the second term loan divided by the applicable exercise price.

The loan proceeds were allocated based on the relative fair values of the debt instrument and the warrant instrument. The fair value of the warrants and the closing costs were recorded as debt discounts and are being amortized using the effective interest rate method over the term of the loan. The effective annual interest rate of the outstanding debt is approximately 11.28% as of December 31, 2019. The Company recognized $1,761 and $1,169 of interest expense related to the loan agreement during the years ended December 31, 2019 and 2018, respectively, including $362 and $360 related to the accretion of the debt discounts and deferred financing costs during the years ended December 31, 2019 and 2018, respectively.

(In thousands, except share and per share data)

Scheduled principal payments on outstanding debt, as of December 31, 2019, are as follows:

Year Ending December 31,	
2020	6,207
2021	6,207
2022	1,552
	$ 13,966

(14) Quarterly Financial Data (unaudited)

	Three months ended			
	December 31, 2019	September 30, 2019	June 30, 2019	March 31, 2019
Revenue	$ —	$ —	$ —	$ 37
Total operating expenses	(23,178)	(30,999)	(27,378)	(20,503)
Net loss and comprehensive loss	(23,641)	(31,271)	(27,638)	(20,580)
Net loss attributable to ordinary shareholders	(23,641)	(31,271)	(27,638)	(20,580)
Net loss per share attributable to ordinary shareholders – basic and diluted	$ (1.59)	$ (2.15)	$ (1.93)	$ (1.44)
Weighted average ordinary shares outstanding – basic and diluted	14,866,838	14,571,278	14,340,231	14,290,437

	Three months ended			
	December 31, 2018	September 30, 2018	June 30, 2018	March 31, 2018
Revenue	$ 239	$ 254	$ 185	$ 191
Total operating expenses	(24,183)	(25,240)	(15,611)	(12,394)
Net loss and comprehensive loss	(24,258)	(24,905)	(15,747)	(12,146)
Net loss attributable to ordinary shareholders	(24,258)	(24,905)	(15,747)	(12,146)
Net loss per share attributable to ordinary shareholders – basic and diluted	$ (1.72)	$ (1.77)	$ (2.22)	$ (61.36)
Weighted average ordinary shares outstanding – basic and diluted	14,108,604	14,034,631	7,085,655	197,949

(15) Subsequent Events

On January 21, 2020, the Company completed a private placement pursuant to which its wholly owned subsidiary, Iterum Bermuda issued and sold approximately $51.6 million aggregate principal amount of Exchangeable Notes and $0.1 million aggregate principal amount of RLNs to a group of accredited investors. The Securities were sold in Units with each Unit consisting of and Exchangeable Note in the original principal amount of $1,000 and 50 RLNs. The Units were sold at a price of $1,000 per Unit. The Exchangeable Notes are exchangeable for the Company's ordinary shares at an initial exchange rate of 1,000 shares per $1,000 of principal and interest on the Exchangeable Notes (equivalent to an initial exchange price of approximately $1.00 per ordinary share), subject to specified limitations. The RLNs entitle holders to payments based on a percentage of the Company's net revenues from potential U.S. sales of specified sulopenem products, subject to the terms and conditions of the indenture governing the RLNs. Pursuant to the indenture governing the RLNs, the payments on the RLNs will be up to either 15% or 20% of net revenues from U.S. sales of such products, depending on the indication approved by the FDA. The aggregate amount of payments on each RLN is capped at $160.00 (or 4,000 times the principal amount of such RLN). Iterum Bermuda received net proceeds from the sale of the Securities of approximately $46.7 million, after deducting placement agent fees and estimated offering expenses.

The Units were issued by Iterum Bermuda, which was formed on November 6, 2019 and is a 100% owned "finance subsidiary" of the Company under Rule 3-10 of Regulation S-X with no independent function other than financing activities. Iterum Therapeutics plc, as the parent company, has no independent assets or operations, and its operations are conducted solely through its

subsidiaries. The Company and each of its subsidiaries other than Iterum Bermuda (the "Subsidiary Guarantors") have provided a full and unconditional guarantee of Iterum Bermuda's obligations under the Exchangeable Notes and the RLNs, and each of the guarantees constitutes the joint and several obligations of the applicable guarantor. The Subsidiary Guarantors are 100% directly or indirectly owned subsidiaries of the Company. There are no significant restrictions upon the Company's or the Subsidiary Guarantors' ability to obtain funds from their subsidiaries by dividend or loan. None of the assets of Iterum Bermuda or the Subsidiary Guarantors represent restricted net assets pursuant to Rule 4-08(e)(3) of Regulation S-X.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2019. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2019, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), we conducted an evaluation of the effectiveness of our internal control over financial reporting. We used the 2013 framework in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission to evaluate the effectiveness of our internal control over financial reporting. Based on our evaluation under that framework, our management has concluded that our internal control over financial reporting was effective as of December 31, 2019.

Our independent registered public accounting firm has not performed an evaluation of our internal control over financial reporting during any period in accordance with the provisions of the Sarbanes-Oxley Act. For as long as we remain an ''emerging growth company'' as defined in Rule 12b-2 of the Exchange Act, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the year ended December 31, 2019, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Code of Ethics

We have adopted a written Code of Business Conduct and Ethics that applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The Code of Business Conduct and Ethics is available on our website at www.iterumtx.com. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website or in a Current Report on Form 8-K.

Directors

The following table sets forth information regarding our directors as of February 29, 2020:

Name	Age	Position
Corey N. Fishman	55	Director, Chief Executive Officer
Brenton K. Ahrens(2)	57	Director, Interim Chairman of the Board
Mark Chin(1)(2)	38	Director
Patrick J. Heron(3)	49	Director
Ronald M. Hunt(1)(3)	55	Director
David G. Kelly(2)(3)	59	Director
Shahzad Malik, M.D.(1)(3)	53	Director

(1) Member of the compensation committee
(2) Member of the audit committee
(3) Member of the nominating and corporate governance committee

Corey N. Fishman has served as our Chief Executive Officer and member of our board of directors since November 2015. From August 2010 to February 2015, Mr. Fishman served as chief operating officer of Durata Therapeutics, Inc., a pharmaceutical company acquired by Actavis plc, a pharmaceutical company, and he also served as chief financial officer of Durata Therapeutics, Inc., from June 2012 to February 2015. From 2008 to 2010, Mr. Fishman served as chief financial officer of GANIC Pharmaceuticals, Inc., a pharmaceutical company. From 2002 to 2008, Mr. Fishman served in a variety of roles at MedPointe Healthcare, Inc., a specialty pharmaceutical company acquired by Meda AB, including as chief financial officer from 2006 to 2008. Mr. Fishman currently serves as a member of the board of directors of Momenta Pharmaceuticals, Inc., a biotechnology company. Mr. Fishman holds a B.A. in economics from the University of Illinois at Urbana-Champaign and an M.S.M. in finance from the Krannert School of Management at Purdue University. We believe Mr. Fishman is qualified to serve on our board of directors due to his role as a founder of our Company, his deep knowledge of our Company and his extensive background in the pharmaceutical industry.

Brenton K. Ahrens has served as a member of our board of directors since November 2015. Since 1999, Mr. Ahrens has served as a general partner with Canaan Partners LLP, a venture capital firm. Prior to joining Canaan Partners, Mr. Ahrens worked in both commercial and technical roles at General Surgical Innovations, a biotechnology company, Ethicon (J&J), a medical device company, and IAP Research, an engineering company. Mr. Ahrens previously served on the board of directors of Durata Therapeutics, Inc., and continues to serve on a number of other private pharmaceutical and healthcare company boards. Mr. Ahrens holds a B.S. and an M.S. in mechanical engineering from the University of Dayton and an M.B.A. from the Tuck School of Business at Dartmouth College. We believe Mr. Ahrens is qualified to serve on our board of directors due to his investment experience, including service on the boards of directors of other healthcare companies.

Mark Chin has served as a member of our board of directors since May 2017. Since August 2016, Mr. Chin has served as an investment manager at Arix Bioscience plc, a life science investment company. From September 2012 to July 2016, Mr. Chin served as a principal at Longitude Capital LLC, a healthcare venture capital firm. From January 2011 to September 2012, Mr. Chin served as a consultant with the Boston Consulting Group. Mr. Chin currently serves on the board of Harpoon Therapeutics, Inc., a clinical-stage immunotherapy company. Mr. Chin has a B.S. in management science from the University of California at San Diego, an M.B.A. from the Wharton School at the University of Pennsylvania and an M.S. in biotechnology from the University of Pennsylvania. We believe Mr. Chin is qualified to serve on our board of directors due to his investment experience in biotechnology and medical technology industries.

Patrick J. Heron has served as a member of our board of directors since November 2015. Since 1999, Mr. Heron has served as a general partner with Frazier Healthcare Partners, a venture capital firm. Prior to joining Frazier Healthcare Partners, Mr. Heron worked at the management consulting firm McKinsey & Company. Before McKinsey, Mr. Heron held positions with Massachusetts General Hospital and biotechnology firm Cetus Corporation. Mr. Heron previously served on the boards of directors of pharmaceutical companies Tobira Therapeutics, Inc., Cidara Therapeutics, Inc., Silvergate Pharmaceutical, Inc., Recida Therapeutics, Inc. and Collegium Pharmaceuticals, Inc. and continues to serve on the boards of directors of the following biotechnology companies: Imago BioSciences, Amunix Therapeutics, SutroVax, Inc., Arcutis Biotherapeutics, Inc., Scout Bio, Inc., Passage Bio, Inc. and Mirum Pharmaceuticals, Inc. Mr. Heron holds a B.A. in political science from the University of North Carolina at Chapel Hill and received an M.B.A. from Harvard Business School. We believe Mr. Heron is qualified to serve on our board of directors due to his extensive business experience, his experience in investing, and his experience in the life sciences industry.

Ronald M. Hunt has served as a member of our board of directors since November 2015. Since 2005, Mr. Hunt has served as a managing director and member of New Leaf Venture Partners, L.L.C., a venture capital firm. Previously, Mr. Hunt served at the Sprout Group, a venture capital firm and was a consultant with consulting firms Coopers & Lybrand Consulting and The Health Care Group. Mr. Hunt also previously served in various sales and marketing positions at Johnson & Johnson and SmithKline Beecham Pharmaceuticals. Mr. Hunt currently serves as a board member of Harpoon Therapeutics, Inc., a clinical-stage immunotherapy company and on the boards of a number of private pharmaceutical and healthcare companies. Mr. Hunt previously served on the board of directors of Neuronetics, Inc. Mr. Hunt holds a B.S. from Cornell University and an M.B.A. from the Wharton School of the University of Pennsylvania. We believe Mr. Hunt is qualified to serve on our board of directors due to his investment experience, his experience in the pharmaceuticals industry and his service on the boards of directors of other biopharmaceutical companies.

David G. Kelly has served as a member of our board of directors since August 2016. From September 2014 to January 2020, Mr. Kelly served as the executive vice president, Ireland of Horizon Therapeutics, plc, a biopharmaceutical company. Mr. Kelly served as managing director, Ireland of Horizon Therapeutics, plc until July 2018. From February 2012 to September 2014, Mr. Kelly served as chief financial officer of Vidara Therapeutics Inc., a pharmaceutical company. From May 2005 to January 2012, Mr. Kelly served as chief financial officer of AGI Therapeutics plc, a pharmaceutical company. Mr. Kelly also served as senior vice president, finance and planning of Warner Chilcott plc (formerly Galen Holdings plc), a pharmaceutical company listed on the London Stock Exchange (LSE). In addition, Mr. Kelly held roles at Elan Corporation, a pharmaceutical company, and KPMG. Mr. Kelly holds a B.A. in economics from Trinity College, Dublin and is also a member of the Institute of Chartered Accountants in Ireland (ACA). We believe Mr. Kelly is qualified to serve on our board of directors due to his experience as a senior executive, particularly within the life science industry, including his experience in finance.

Shahzad Malik, M.D. has served as a member of our board of directors since May 2017. Since 1999, Dr. Malik has served as a general partner at Advent Life Sciences LLP, a venture capital firm. Prior to joining Advent, Dr. Malik spent six years practicing medicine before joining the London office of McKinsey & Company, a management consulting firm. Dr. Malik previously served on the boards of directors of Conatus Pharmaceuticals Inc., a pharmaceutical company, Agenus Inc., a biotechnology company, Aravive, Inc. (formerly Versartis, Inc.), a biopharmaceutical company, and Axonics Modulation Technologies, Inc., a medical technology company. Dr. Malik continues to serve on the boards of directors of a number of other private pharmaceutical and healthcare company boards. Dr. Malik holds an M.A. from Oxford University and an M.D. from Cambridge University. He subsequently specialized in interventional cardiology while also pursuing research interests in heart muscle disorders both in the clinic and basic science laboratory. We believe Dr. Malik is qualified to serve on our board of directors due to his experience practicing medicine and his investment experience.

Executive Officers

The following table sets forth information regarding our executive officers as of February 29, 2020:

Name	Age	Position
Corey N. Fishman	55	Director, Chief Executive Officer
Michael W. Dunne	60	Chief Scientific Officer
Judith M. Matthews	50	Chief Financial Officer

In additon to the biographical information for Mr. Fishman, which is set forth above, set forth below is certain biographical information about Dr. Dunne and Ms. Matthews:

Michael W. Dunne, M.D. has served as our Chief Scientific Officer since November 2015. From November 2014 until September 2015, Dr. Dunne was vice president research and development at Actavis. From September 2010 to October 2014, Dr. Dunne served as chief medical officer of Durata Therapeutics, Inc., where he previously served as acting chief medical officer on a consulting basis from December 2009 to September 2010. From 1992 to 2009, Dr. Dunne served in a variety of roles in connection with the clinical development of numerous infectious disease compounds at Pfizer Inc., a biopharmaceutical company, including as the vice president, therapeutic head of development for infectious disease from 2001 to 2009. Dr. Dunne holds a B.A. in economics from Northwestern University and an M.D. from the State University of New York Health Sciences Center. He completed his internal medicine residency and fellowships in infectious diseases and pulmonary medicine at Yale University School of Medicine.

Judith M. Matthews has served as our Chief Financial Officer since November 2015. From 2012 to February 2015, Ms. Matthews served as vice president of finance at Durata Therapeutics, Inc. From 2009 to 2012, Ms. Matthews served as head of financial planning & analysis at Bally Total Fitness Corporation, a fitness club chain. From 2004 to 2008, Ms. Matthews served as vice president of finance for the Sterno Group, a subsidiary of Blyth, Inc., a home products company. Ms. Matthews holds a B.A. in accounting from the University of Illinois at Urbana-Champaign and a Master of Management in finance and marketing from the Kellogg School of Management at Northwestern University.

Audit Committee

Our audit committee consists of David G. Kelly (Chairman), Brenton K. Ahrens and Mark Chin. The chairperson of our audit committee is Mr. Kelly.

Our board of directors has determined that Messrs. Kelly, Ahrens and Chin each satisfy the independence standards for such committees established by the SEC and the Nasdaq Stock Market.

Our board of directors has determined that Mr. Kelly is an "audit committee financial expert" within the meaning of SEC regulations. Our board of directors has also determined that each member of our audit committee has the requisite financial expertise required under the applicable requirements of the Nasdaq Stock Market. In arriving at this determination, the board of directors has examined each audit committee member's scope of experience and the nature of their employment in the corporate finance sector.

Director Designation Rights

Pursuant to the terms of an investor rights agreement (the 2020 Investor Rights Agreement) that we entered into in January 2020 with the purchasers in the January 2020 private placement pursuant to which our wholly owned subsidiary, Iterum Therapeutics Bermuda Limited, sold units consisting of (i) 6.500% Exchangeable Senior Subordinated Notes due 2025 and (ii) Limited Recourse Royalty-Linked Subordinated Notes, for so long as Sarissa Capital Management LP (Sarissa) and its affiliates own at least 5% or 12.5%, as applicable, of our outstanding ordinary shares on a fully diluted basis, promptly, and in any event no more than 5 business days following written request of Sarissa, we will cause our board of directors to increase to consist of nine or 10 members, as applicable, and we will cause the board of directors to consist of no more than 10 members without the prior written consent of Sarissa. In addition, for so long as Sarissa and its affiliates own at least 12.5% of our outstanding ordinary shares on a fully diluted basis, Sarissa will have the right to designate two directors to our board of directors and, for so long as Sarissa and its affiliates own at least 5% but less than 12.5%, it will have the right to designate one director to our board of directors (Investor Designees). Pursuant to the terms of the 2020 Investor Rights Agreement, such Investor Designees will be appointed to our board of directors and to be members of the class of directors that was subject to reelection at our most recent annual meeting of shareholders. The Investor Designees will be entitled to be a member of any committee of our board of directors subject to the terms of the 2020 Investor Rights Agreement. Pursuant to the terms of the 2020 Investor Rights Agreement, the purchasers party thereto, subject to specified exceptions, have agree with us to vote in favor of the election of the Investor Designees, and we have agreed to cause the Investor Designees to be named in any relevant proxy statement.

Item 11. Executive Compensation.

The following discussion provides details of the compensation and other benefits paid by us and our subsidiaries to certain executive officers for services provided for the years ended December 31, 2019 and 2018 and to the members of our board of directors for services provided for the year ended December 31, 2019.

Executive and Director Compensation Processes

Our executive compensation program is administered by our compensation committee, subject to oversight by our board of directors. Our compensation committee reviews our executive compensation practices on an annual basis and approves, or recommends for approval by the board, the compensation of the Company's executives.

Our compensation committee periodically reviews and makes recommendations to the board of directors with respect to director compensation.

For the years ended December 31, 2019 and 2018, at the direction of our compensation committee, our Company retained Frederic W. Cook & Co., Inc, or FW Cook, as an independent compensation consultant to provide comparative data on executive compensation practices in our industry and to provide advice to the compensation committee in relation to our executive compensation program generally, including advice and recommendations on the amounts and forms of executive compensation. While FW Cook provides advice to the company and the compensation committee in relation to such compensation practices, the compensation committee ultimately makes its own decisions with regard to our executive and director compensation programs.

The compensation committee reviewed information regarding the independence and potential conflicts of interest of FW Cook, taking into account, among other things (i) the provision of other services to the Company by FW Cook; (ii) the amount of fees received by FW Cook from the Company as a percentage of its total revenue; (iii) FW Cook's policies and procedures to prevent conflicts of interest; (iv) any business or personal relationships that FW Cook has with any member of the compensation committee; (v) any shares held by FW Cook in the Company; and (vi) any business or personal relationship FW Cook or FW Cook employees have with any executive officers of the Company. Based on this review, the compensation commitee concluded that the engagement did not raise any conflict of interest.

Executive Officer Summary Compensation Table

The following table provides details of the compensation and other benefits paid or accrued by us and our subsidiaries to our President and Chief Executive Officer and our two next most highly compensated executive officers, Mr. Michael W. Dunne M.D., our Chief Scientific Officer, and Ms. Judith M. Matthews, our Chief Financial Officer for services provided for the years ended December 31, 2019 and 2018:

Name and Principal Position	Year Ended December 31,	Salary ($)	Share Awards[1] ($)	Option Awards[1] ($)	Non-Equity Incentive Plan Compensation[2] ($)	All Other Compensation[3] ($)	Total ($)
Corey N. Fishman	2019	551,138	123,150	561,000	151,841	4,902	1,392,031
President and Chief Executive Officer	2018	494,546	—	953,529	305,910	2,622	1,756,607
Michael W. Dunne, M.D.	2019	402,794	73,890	317,900	81,000	7,524	883,108
Chief Scientific Officer	2018	377,606	—	595,957	166,551	4,902	1,145,016
Judith M. Matthews	2019	356,417	32,840	112,200	62,475	1,161	565,093
Chief Financial Officer	2018	305,707	—	178,786	126,175	995	611,663

(1) The amounts reported do not reflect the amounts actually received by our executive officers. Instead, these amounts reflect the aggregate grant date fair values of performance restricted share units and share options granted to our executive officers during the years ended December 31, 2019 and 2018, respectively, as computed in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, 718. Assumptions used in the calculation of these amounts are included in Note 10 to our audited financial statements included in this 10-K. As required by SEC rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions. Our executive officers who have received options will only realize compensation with regard to these options to the extent the trading price of our ordinary shares is greater than the exercise price of such options.

(2) Amount represents cash bonuses earned for the 12-month periods ending December 31, 2019 and 2018, respectively. Amounts disclosed for the year ended December 31, 2019 exclude payments made in 2019 for 2018 bonuses. Amounts disclosed for the year ended December 31, 2018 exclude payments made in 2018 for 2017 bonuses.

(3) Includes the dollar value of life insurance premiums paid by the company for the benefit of such executive.

Narrative Disclosure to Executive Officer Summary Compensation Table

Base Salary

During the year ended December 31, 2019, we paid base salaries of $551,138 to Mr. Fishman, $402,794 to Dr. Dunne and $356,417 to Ms. Matthews. During the year ended December 31, 2018, we paid base salaries of $494,546 to Mr. Fishman, $377,606 to Dr. Dunne and $305,707 to Ms. Matthews.

In February 2020, our compensation committee approved, consistent with the recommendations of the compensation committee's independent compensation consultant who, in 2020, was CODA Advisors, LLC, an increase to the base salaries of Mr.

Fishman, Dr. Dunne and Ms. Matthews as follows: $561,813 for Mr. Fishman, $412,088 for Dr. Dunne and $363,248 for Ms. Matthews.

None of the named executive officers are currently party to any employment arrangements that provide for automatic or scheduled increases in base salary.

Non-Equity Incentive Plan Compensation

Our named executive officers participate in a cash bonus program which is tied to the achievement of strategic and corporate goals of the Company, which are approved annually by our compensation committee. Our compensation committee determines the amount of these bonuses, if any, based on its assessment of the named executive officers' performance and that of the Company against goals established annually.

Under their respective employment agreements, the annual target bonus for Mr. Fishman is 55% of his current base salary, the annual target bonus for Dr. Dunne is 40% of his current base salary and the annual target bonus for Ms. Matthews is 35% of her current base salary.

At the beginning of each year, our compensation committee reviews the accomplishments of the named executive officers as measured against the the previous year's goals, whether each goal had been achieved and the relative weight that should be given to each goal in determining the cash bonus payment for that year. Based on its review, the compensation committee recommended cash bonus payments of $151,841 to Mr. Fishman, $81,000 to Dr. Dunne and $62,475 to Ms. Matthews with respect to the year ended December 31, 2019. The compensation committee recommended cash bonus payments of $305,910 to Mr. Fishman, $166,551 to Dr. Dunne and $126,175 to Ms. Matthews with respect to the year ended December 31, 2018.

Equity Incentive Awards

We believe that our ability to grant equity-based awards is a valuable and necessary compensation tool that aligns the long-term financial interests of our executive officers and our shareholders. In addition, we believe that our ability to grant options and other equity-based awards helps us to attract, retain and motivate our executive officers and encourages them to devote their best efforts to our business and financial success.

In February 2020, pursuant to powers delegated to it by the board of directors, our compensation committee approved the grant of performance restricted stock units, or PSUs, under our 2018 Equity Incentive Plan to our named executive officers which are subject to certain performance based vesting conditions. The following number of PSUs were granted to the executive officers: 335,000 to Mr. Fishman, 160,000 to Dr. Dunne and 125,000 to Ms. Matthews. These PSUs shall vest in the following proportions: (i) 50% upon Board certification of the acceptance by the United States Food and Drug Administration, or the FDA, of a New Drug Application, or NDA,, provided such event occurs on or before December 31, 2021; and (ii) 50% on the date which is the initial deadline set by the FDA to complete its review of such NDA in accordance with the Prescription Drug User Fee Act, provided such event occurs on or before December 31, 2021 and in each case such executive remains in continued service with us.

In January 2019, our compensation committee approved the grant of share options under the 2018 Equity Incentive Plan to the named executive officers to purchase the following number of shares, effective on February 15, 2019: 150,000 to Mr. Fishman, 85,000 to Dr. Dunne and 30,000 to Ms. Matthews. 25% of each option vested on February 15, 2020 based on each named executive officer's continued service with us through that date and the remaining 75% is scheduled to vest in equal monthly installments thereafter until February 15, 2023 subject to each named executive officer's continued provision of services to us on each vesting date. Each of the option awards has an exercise price of $5.80 per share, being the closing price on the Nasdaq Global Market on the date of grant.

In January 2019, the compensation committee also approved the grant of performance restricted stock units, or PSUs, under our 2018 Equity Incentive Plan to our named executive officers effective on February 15, 2019 and which are subject to certain performance based vesting conditions. The following number of PSUs were granted to the executive officers: 15,000 to Mr. Fishman, 9,000 to Dr. Dunne and 4,000 to Ms. Matthews. The vesting of these PSUs is subject to approval of an NDA of ours by the FDA and achievement of our ordinary shares on the Nasdaq Global Market of an average closing price that equals or exceeds $13 over any 20 consecutive trading days (from the period beginning 19 days prior to receipt of NDA approval) at a point in time when the executive remains in continued service with us and provided such events occur on or before December 31, 2021.

In March 2018, the board of directors approved the grant of stock options under the 2018 Equity Incentive Plan to the named executive officers to purchase the following number of shares, effective on our initial public offering: 127,307 to Mr. Fishman, 79,567 to Dr. Dunne and 23,870 to Ms. Matthews. 25% of the options vested on May 24, 2019 with the remaining 75% scheduled to vest in equal monthly installments thereafter until May 24, 2022 subject to each named executive officer's continued provision of services to

us on each vesting date. Each of the option awards has an exercise price of $13.00 per share, being the closing price on the Nasdaq Global Market on the date of grant.

Outstanding Equity Awards at December 31, 2019

The following table presents information regarding outstanding equity awards held by our named executive officers as of December 31, 2019. All equity awards were granted under our 2015 Equity Incentive Plan and our 2018 Equity Incentive Plan.

	Option Awards				Share Awards	
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable(1)	Option Exercise Price Per Share(2)	Option Expiration Date	Equity incentive plan awards: Number of unearned shares, units or other rights that have not vested(3) (#)	Equity incentive plan awards: Market or payout value of unearned shares, units or other rights that have not vested ($)
Corey N. Fishman	36,759	28,592(4)	$3.30	09/11/2027	—	—
	50,392	76,915(5)	13.00	05/23/2028	—	—
	—	150,000(6)	5.80	02/14/2029	—	—
	—	—	—	12/31/2021	15,000	67,500
Michael W. Dunne, M.D.	23,392	18,195 (4)	3.30	09/11/2027	—	—
	31,495	48,072 (5)	13.00	05/23/2028	—	—
	—	85,000 (6)	5.80	02/14/2029	—	—
	—	—	—	12/31/2021	9,000	40,500
Judith M. Matthews	6,683	5,199 (4)	3.30	09/11/2027	—	—
	9,448	14,422 (5)	13.00	05/23/2028	—	—
	—	30,000 (6)	5.80	02/14/2029	—	—
	—	—	—	12/31/2021	4,000	18,000

(1) Pursuant to the equity agreements between the named executive officer and us, the vesting of such named executive officer's share and option awards will accelerate under certain circumstances as described under the section titled "—Potential Payments Upon Termination or Change in Control

(2) The exercise price per share of the stock options reflects the fair market value per ordinary share on the date of grant.

(3) The awards reported are performance restricted share units for which vesting is subject to approval of an NDA of ours by the FDA and achievement of our ordinary shares on the Nasdaq Global Market of an average closing price that equals or exceeds $13 over any 20 consecutive trading days (from the period beginning 19 days prior to receipt of NDA approval) at a point in time when the executive remains in continued service with us and provided that each such event occurs on or before December 31, 2021.

(4) Stock option that vested as to 1/4th of the shares underlying the option on September 12, 2018 with the remaining shares scheduled to vesting in equal monthly installments thereafter until September 12, 2021, subject to continued service with us through each relevant vesting date.

(5) Stock option that vested as to 1/4th of the shares underlying the option on May 24, 2019 with the remaining shares scheduled to vesting in equal monthly installments thereafter until May 24, 2022, subject to continued service with us through each relevant vesting date.

(6) Stock option that vested as to 1/4th of the shares underlying the option on February 15, 2020 with the remaining shares scheduled to vesting in equal monthly installments thereafter until February 15, 2023, subject to continued service with us through each relevant vesting date.

Employment Agreements with Executive Officers

We have entered into offer letters with each of our named executive officers. The offer letters generally provide for at-will employment and set forth the executive's initial base salary, target variable compensation, eligibility for employee benefits, the terms of initial equity grants and in some cases severance benefits on a qualifying termination. Each of our named executive officers has also executed our standard form proprietary information agreement. Any potential payment and benefits due upon a termination of employment or change of control of us are further described below.

Corey N. Fishman serves as our President and Chief Executive Officer. On November 18, 2015, Mr. Fishman entered into an offer letter with Iterum Therapeutics US Limited, our indirect wholly owned subsidiary. The offer letter has no specific term and constitutes an at-will employment arrangement. In 2017, Mr. Fishman's base salary was $420,000. On May 2, 2018, Mr. Fishman entered into an amended offer letter, which became effective upon the closing of our initial public offering pursuant to which Mr. Fishman's base salary became $540,000, and his discretionary annual target performance bonus increased from 50% to 55% of his annual base salary. His base salary was reviewed in January 2019 and increased to $552,150, effective February 1, 2019. His base salary was reviewed in February 2020 and increased to $561,813, effective February 1, 2020.

Michael W. Dunne, M.D. serves as our Chief Scientific Officer. On November 18, 2015, Dr. Dunne entered into an offer letter with Iterum Therapeutics US Limited, our indirect wholly owned subsidiary. The offer letter has no specific term and constitutes an at-will employment arrangement. Dr. Dunne's base salary pursuant to the offer letter was $350,000 and his discretionary annual target performance bonus is 40% of his annual base salary. In 2017, Dr. Dunne's base salary was $367,500 and in 2018 was $378,525. Dr.

Dunne's base salary was reviewed in January 2019 and was increased to $405,000, effective February 1, 2019. His base salary was reviewed in February 2020 and increased to $412,088, effective February 1, 2020.

Judith M. Matthews serves as our Chief Financial Officer. On November 18, 2015, Ms. Matthews entered into an offer letter with Iterum Therapeutics US Limited, our indirect wholly owned subsidiary. The offer letter has no specific term and constitutes an at-will employment arrangement. In 2017, Ms. Matthew's base salary was $236,250. Ms. Matthews entered into an amended offer letter, which became effective upon the closing of our initial public offering pursuant to which Ms. Matthews' base salary became $350,000, and her discretionary annual target performance bonus increased from 25% to 35% of her annual base salary. Ms. Matthew's base salary was reviewed in January 2019 and increased to $357,000, effective February 1, 2019. Her base salary was reviewed in February 2020 and increased to $363,248, effective February 1, 2020.

Potential Payments Upon Termination or Change in Control

Our agreements with each of our named executive officers provide that upon the termination of his or her employment by us other than for cause, or by the named executive officer with good reason (each as defined in the offer letters), he or she will be entitled to receive the following severance benefits:

- cash severance equal to a fixed number of months of such executive's base salary (twelve months in the case of Mr. Fishman and nine months in the case of Dr. Dunne and Ms. Matthews); and
- Company-paid COBRA premiums for up to 12 months following such executive's termination date.

If such a qualifying termination occurs within the period beginning one month prior to and ending 12 months following a change of control of us, the cash severance payment entitlement described above will increase to twelve months of such executive's then current base salary in the case of Dr. Dunne and Ms. Matthews, and to eighteen months of his then current base salary in the case of Mr. Fishman. The executives will also be entitled to an additional cash payment equal to a percentage of such executives' target annual bonus for the year of termination, equal to 100% in the case of Dr. Dunne and Ms. Matthews and 150% in the case of Mr. Fishman. In addition, each of Mr. Fishman, Dr. Dunne and Ms. Matthews' currently outstanding share awards will accelerate in full.

Each offer letter also contains a "better after-tax" provision, which provides that if any of the payments to such named executive officer constitutes a parachute payment under Section 280G of the Internal Revenue Code of 1986, as amended, or the Code, the payments will either be (i) reduced or (ii) provided in full to the executive, whichever results in the executive receiving the greater amount after taking into consideration the payment of all taxes, including the excise tax under Section 4999 of the Code, in each case based upon the highest marginal rate for the applicable tax.

Payment of any of the severance benefits described above is also conditioned on the named executive officer's delivery and non-revocation of a general release of claims in our favor.

On March 11, 2020, on recommendation from the compensation committee, our board of directors approved the creation of a carve out plan to reward certain key employees including Mr. Fishman, Dr. Dunne and Ms. Matthews in the event of a change of control. The aggregate amount payable under the plan will be calculated on a tiered basis based on the upfront consideration payable to us and our equityholders in connection with such change of control, with potential aggregate amounts payable under the plan falling within a range around approximately 2.5% of the upfront consideration. The other terms of the plan and each executive's entitlement to participate are to be determined at the time of the change of control transaction.

Director Compensation – Summary Compensation Table

The following table shows the total compensation paid or accrued by us and our subsidiaries during the year ended December 31, 2019 to each of our current and former non-employee directors. Directors who are employed by us are not compensated for their service on our board of directors.

Name	Fees Earned or Paid in Cash ($)	Share Awards(1)(2) ($)	Option Awards (1)(3) ($)	Other Compensation(6) ($)	Total ($)
Brenton K. Ahrens	42,500	—	80,000	—	122,500
Mark Chin	48,500	40,000	—	40,000	128,500
Paul R. Edick(4)	38,250	—	—	—	38,250
James I. Healy M.D., Ph.D.(5)	41,000	40,000	-	40,000	121,000
Patrick J. Heron	39,000	20,000	40,000	20,000	119,000
Ronald M. Hunt	51,000	40,000	—	40,000	131,000
David G. Kelly	59,000	80,000	—	—	139,000
Shahzad Malik, M.D.	45,000	—	80,000	—	125,000

(1) The amounts reported do not reflect the amounts actually received by our director. Instead, these amounts reflect the aggregate grant date fair values of restricted share units and stock options granted to our directors during the years ended December 31, 2019, as computed in accordance with FASB ASC 718. Assumptions used in the calculation of these amounts are included in Note 10 to our audited financial statements included in this 10-K. As required by SEC rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions. Our directors who have received options will only realize compensation with regard to these options to the extent the trading price of our ordinary shares is greater than the exercise price of such options.
(2) The aggregate number of outstanding restricted share units held by each of our non-employee directors as of December 31, 2019 were as follows: Mr. Ahrens: 0; Mr. Chin: 5,703; Mr. Edick: 0; Dr. Healy: 5,703; Mr. Heron: 2,852; Mr. Hunt: 5,703; Mr. Kelly: 11,406; and Dr. Malik: 0.
(3) The aggregate number of shares subject to outstanding share options units held by each of our non-employee directors as of December 31, 2019 were as follows: Mr. Ahrens: 19,671; Mr. Chin: 0; Mr. Edick: 0; Dr. Healy: 0; Mr. Heron: 9,836; Mr. Hunt: 11,241; Mr. Kelly: 3,182; and Dr. Malik: 30,912.
(4) Mr. Edick did not stand for reelection to our board of directors at our 2019 Annual General Meeting of Shareholders held on June 13, 2019 and his service as a director ceased on the date of such meeting.
(5) Dr. Healy resigned as a member of our board of directors on February 12, 2020.
(6) With respect to the portion of equity compensation to be made in restricted stock units, directors can elect for the award to be made in the form of a mixture of 50% cash and 50% shares on vesting. Other compensation represents that portion of the restricted stock units elected to be made in the form of cash.

On the expiry of Paul R. Edick's term of office as director on June 13, 2019, pursuant to an ordinary share subscription deed dated as of October 14, 2015 between us and Mr. Edick, the compensation committee approved the acceleration of all remaining unvested ordinary shares issued thereunder, being 331 ordinary shares. As a result, those ordinary shares were no longer subject to a right of repurchase by us. In addition, the compensation committee approved the acceleration of 1,060 options over ordinary shares held by Mr. Edick at a price of $3.30 such that on the expiry of his term as director, those share options became exercisable in full.

Non-Employee Director Compensation Policy

Under our Non-Employee Director Compensation Policy each non-employee director is eligible to receive compensation for his or her service consisting of annual cash retainers and equity awards. Each director receives an annual base cash retainer of $35,000 for such service, to be paid quarterly. The non-executive chairperson of our board of directors receives an additional annual base cash retainer of $27,500 for such service, to be paid quarterly.

The policy also provides that we compensate the members of our board of directors for service on our committees as follows:

- The chairperson of our audit committee receives an annual cash retainer of $15,000 for such service, paid quarterly, and each of the other members of the audit committee receives an annual cash retainer of $7,500, paid quarterly.
- The chairperson of our compensation committee receives an annual cash retainer of $12,000 for such service, paid quarterly, and each of the other members of the compensation committee receives an annual cash retainer of $6,000, paid quarterly.
- The chairperson of our nominating and corporate governance committee receives an annual cash retainer of $8,000 for such service, paid quarterly, and each of the other members of the nominating and corporate governance committee receives an annual cash retainer of $4,000, paid quarterly.

The policy further provides for the grant of annual equity awards as follows:

- Each director will receive annual equity awards with a fixed value of $80,000.
- The equity awards will be granted as a mix of share options and restricted stock units, at such director's discretion. Each director must determine their mix of equity awards no later than 30 days prior to the applicable grant date.
- All equity awards will vest on the one-year anniversary of the grant date.
- The value of a share option to be granted under this policy will be determined using the same method we use to calculate the grant-date fair value of share options in our financial statements, except that no provision will be made for estimated forfeitures related to service-based vesting. The actual number of shares to be granted under a restricted stock unit award under this policy will be determined by dividing the grant date value by a 30-day volume weighted average trading price (ending on the trading day immediately preceding the grant date).

We also reimburse our non-employee directors for reasonable travel and other expenses incurred in connection with attending our board of director and committee meetings.

For 2020, it was agreed that the right to receive an annual equity award would be waived by each of the non-executive directors with the exception of Mr. Kelly.

Risk Considerations in Our Compensation Program

Our compensation committee has reviewed and evaluated the philosophy and standards on which our compensation plans have been developed and implemented across our Company. It is our belief that our compensation programs do not encourage inappropriate actions or risk taking by our executive officers. We do not believe that any risks arising from our employee compensation policies and practices are reasonably likely to have a material adverse effect on our Company. In addition, we do not believe that the mix and design of the components of our executive compensation program encourage management to assume excessive risks.

2018 Equity Incentive Plan

Our board of directors adopted our 2018 Equity Incentive Plan, or the 2018 Plan, in March 2018 and our shareholders approved the 2018 Plan in May 2018.

Authorized Awards. Our 2018 Plan authorizes the award of incentive stock options that may qualify for favorable tax treatment under U.S. tax laws to their recipients under Section 422 of the Code, or ISOs, nonstatutory stock options, or NSOs, stock appreciation rights, or SARs, restricted stock, restricted stock units, or RSUs, performance-based awards, and other stock awards, which are collectively referred to as awards. We may grant awards under the 2018 Plan to our employees, including our officers, and employees of our affiliates. A separate sub-plan to the 2018 Plan has been established for the purpose of granting awards to our non-employee directors and consultants and non-employee directors and consultants of our affiliates, which we refer to as the Sub-Plan. The provisions of the 2018 Plan apply in their entirety to any awards made under the Sub-Plan save for certain amendments set out in the Sub-Plan required in the context of awards to non-employee directors and consultants and non-employee directors and consultants of our affiliates, rather than employees, including references to eligible participants under the Sub-Plan.

Share Reserve. Initially, the aggregate number of our ordinary shares that may be issued pursuant to awards under our 2018 Plan was 1,018,459 shares, which includes any shares subject to outstanding options or other awards that were granted under our 2015 Plan and that are forfeited, terminated, expire or are otherwise not issued. Additionally, upon board or committee approval the number of ordinary shares reserved for issuance under our 2018 Plan will increase on January 1 of each calendar year for ten years, starting on January 1, 2019 and ending on and including January 1, 2028, in an amount up to 4% of the total number of our ordinary shares outstanding on December 31 of the prior calendar year, or a lesser number of shares determined by our board of directors. On December 5, 2018, pursuant to powers delegated to it by our board of directors, the compensation committee approved effective January 1, 2019 an increase in the number of ordinary shares available to be granted pursuant to the 2018 Plan by 4% of the total number of issued share capital on December 31, 2018, being 574,081 ordinary shares. In February 2020, the compensation committee approved an increase in the number of ordinary shares available to be granted pursuant to the 2018 Plan by 594,758. As of December 31, 2019, options to purchase 936,618 ordinary shares were outstanding under our 2018 Plan, with a weighted-average exercise price of $8.97 per share. As of December 31, 2019, there were 31,367 and 50,000 ordinary shares to be issued upon vesting of outstanding RSUs and PSUs, respectively.

The maximum number of our ordinary shares that may be issued upon the exercise of ISOs under our 2018 Plan is equal to 3,055,377.

Shares subject to awards granted under our 2018 Plan that expire or terminate without being exercised in full, or that are paid out in cash rather than in shares, do not reduce the number of shares available for issuance under our 2018 Plan. Additionally, shares become available for future grant under our 2018 Plan if they were issued under awards under our 2018 Plan if we repurchase them or they are forfeited. This includes shares used to pay the exercise price of an award or to satisfy the tax withholding obligations related to an award.

Plan Administration. Our 2018 Plan is administered by our compensation committee, or by our board of directors or another duly authorized committee of our board of directors, acting in place of our compensation committee. Our board of directors or our compensation committee may also delegate to one or more of our officers the authority to designate employees (other than officers) to receive specified share awards, and determine the number of shares subject to such awards.

Our compensation committee has the authority to construe and interpret our 2018 Plan, grant and amend awards, determine the terms of such awards and make all other determinations necessary or advisable for the administration of the plan, including, but not limited to, repricing options or SARs without prior shareholder approval. Awards granted under the 2018 Plan may vest over time based on the holder's continued service with us, or following the achievement of certain pre-established performance goals.

Options. Options represent the right to purchase our ordinary shares on the date of exercise at a stated exercise price. ISOs may only be granted to employees of the Company and its subsidiaries. The exercise price of an option generally must be at least equal to the fair market value of our ordinary shares on the date of grant. Our compensation committee may provide for options to be exercised only as they vest or to be immediately exercisable with any shares issued on exercise being subject to our right of repurchase that lapses as the shares vest. The maximum term of options granted under our 2018 Plan is ten years.

Restricted Stock Awards. Restricted stock awards represent an offer by us to issue or sell our ordinary shares subject to vesting restrictions, which may lapse based on time or achievement of performance conditions. The price (if any) of a restricted stock award will be determined by our compensation committee. Unless otherwise determined by our compensation committee at the time of grant, vesting will cease on the date the participant no longer provides services to us and unvested shares will be forfeited.

Restricted Stock Unit Awards (RSUs) and Performance Restricted Stock Units (PSUs). RSUs and PSUs represent the right to receive our ordinary shares at a specified date in the future, subject to forfeiture of that right because of termination of employment or failure to achieve certain performance conditions. If an RSU/PSU award has not been forfeited, then on the date specified in the RSU/PSU agreement, we will deliver to the holder a number of whole ordinary shares, cash or a combination of our ordinary shares and cash. Additionally, dividend equivalents may be credited in respect of shares covered by an RSU/PSU award.

Stock Appreciation Rights. SARs provide for a payment, or payments, in cash or ordinary shares, to the holder based upon the difference between the fair market value of our ordinary shares on the date of exercise and the stated exercise price. The maximum term of SARs granted under our 2018 Plan is ten years.

Other Stock Awards. Our compensation committee may grant other awards based in whole or in part by reference to our ordinary shares. Our compensation committee will determine the number of shares under such award and all other terms and conditions of such awards.

Transferability. Awards granted under our 2018 Plan may not be transferred in any manner other than by will or by the laws of descent and distribution or as otherwise determined by our compensation committee or under the terms of our 2018 Plan or an applicable award agreement.

Changes to Capital Structure. In the event that there is a specified type of change in our capital structure, such as a share split or recapitalization, appropriate adjustments will be made to (i) the class and the maximum number of shares reserved for issuance under our 2018 Plan, (ii) the class and the maximum number of shares by which the share reserve may increase automatically each year, (iii) the class and the maximum number of shares that may be issued upon the exercise of ISOs, and (iv) the class and the number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding awards.

Corporate Transactions. Our 2018 Plan provides that in the event of certain specified significant corporate transactions, each outstanding award will be treated as determined by our board of directors unless otherwise provided in an award agreement or other written agreement between us and the award holder. The board of directors may take one of the following actions with respect to such awards:

- arrange for the assumption, continuation or substitution of an award by a successor corporation;
- arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation;

- accelerate the vesting, in whole or in part, of the award and provide for its termination prior to the transaction;
- arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us;
- cancel or arrange for the cancellation of the award, to the extent not vested or not exercised prior to the closing of the transaction, in exchange for a cash payment or no payment, as determined by our board of directors; and
- cancel or arrange for the cancellation of the award to the extent not vested but not exercised prior to the closing of the transaction, in exchange for a payment, in the form determined by our board of directors, equal to the excess, if any, of (A) the per share amount payable to holders of our ordinary shares in the transaction over (B) any exercise price payable by the participant in connection with the award, multiplied by the number of shares subject to the award.

- A corporate transaction generally will be deemed to occur in the event of: (i) a sale of all or substantially all of our assets, (ii) the sale or disposition of more than 50% of our outstanding securities, (iii) the consummation of a merger or consolidation where we do not survive the transaction and (iv) the consummation of a merger or consolidation where we do survive the transaction but our ordinary shares outstanding prior to such transaction are converted or exchanged into other property by virtue of the transaction. In addition, any one or more of the above events may be effected pursuant to (x) a takeover under Irish takeover rules; (y) a compromise or arrangement under Chapter 1 of Part 9 of the Irish Companies Act 2014 (Irish Companies Act) or (z) Chapter 2 of Part 9 of the Irish Companies Act.

- The board of directors is not obligated to treat all awards or portions of stock awards, even those that are of the same type, in the same manner.

- *Amendment and Termination*. Our board of directors or another duly authorized committee has the authority to amend, suspend, or terminate our 2018 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our shareholders. No ISOs may be granted after the tenth anniversary of the date our board of directors adopted our 2018 Plan, and no awards may be granted under our 2018 Plan while it is suspended or after it is terminated.

2015 Equity Incentive Plan

- Our board of directors adopted and our shareholders approved our 2015 Equity Incentive Plan, or the 2015 Plan, in November 2015. The 2015 Plan was amended most recently in May 2017. The 2015 Plan provides for the grant of ISOs, NSOs, restricted stock awards, RSUs, SARs, and other stock awards to our employees, directors and consultants.

- Since the 2018 Plan became effective, we no longer grant awards under the 2015 Plan. However, any outstanding awards granted under the 2015 Plan remain outstanding, subject to the terms of the 2015 Plan and stock option agreements, until such outstanding options are exercised or until they terminate or expire by their terms.

- *Authorized Shares*. As of December 31, 2019, options to purchase 213,652 ordinary shares were outstanding under our 2015 Plan, with a weighted-average exercise price of $3.31 per share. As of December 31, 2018, options to purchase 233,607 ordinary shares were outstanding under our 2015 Plan, with a weighted-average exercise price of $3.32 per share. The maximum number of ordinary shares that may be issued on the exercise of ISO under our 2015 Plan is the share reserve.

- *Plan Administration*. Our 2015 Plan may be administered by our board of directors or another duly authorized committee. Our 2015 Plan is currently administered by our compensation committee. Our board of directors or another duly authorized committee has the authority to construe and interpret our 2015 Plan, amend the plan and outstanding awards and make all other determinations necessary or advisable for the administration of the plan, including, but not limited to, repricing options or SARs without prior shareholder approval.

- *Corporate Transactions*. Our 2015 Plan provides that in the event of a corporate transaction, each outstanding award will be treated as determined by our board of directors unless otherwise provided in an award agreement or other written agreement between us and the award holder. The board of directors may generally take the same actions as summarized above in connection with awards under the 2018 Plan, and the definition of a corporate transaction under the 2015 Plan is substantially the same as such defined term in the 2018 Plan.

- *Transferability*. Awards granted under our 2015 Plan may not be transferred in any manner other than by will or by the laws of descent and distribution or as otherwise determined by our compensation committee or under the terms of our 2015 Plan or an applicable award agreement.

- *Plan Amendment or Termination*. Our board of directors or another duly authorized committee has the authority to amend, suspend, or terminate our 2015 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our shareholders.

Health and Welfare Benefits

All of our named executive officers are eligible to participate in our employee benefit plans, including our medical, dental, and vision insurance plans, in each case on the same basis as all of our other full-time employees.

***401(k)* Plan**

We maintain a defined contribution retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees may defer eligible compensation on a pre-tax basis, up to the statutorily prescribed annual limits on contributions under the Code. The Company is required to contribute a deferral rate of up to 3% to the 401(k) plan on behalf of certain employees. We have not historically made discretionary contributions to the 401(k) plan for the benefit of employees. Employee contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participant's directions. Employees are immediately and fully vested in their contributions. The 401(k) plan is intended to be qualified under Section 401(a) of the Code with the 401(k) plan's related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan.

Limitation on Liability and Indemnification of Directors and Officers

Our articles of association, and indemnification agreements with our board of directors and executive officers provide for indemnification for our directors and officers.

Rule 10b5-1* Sales *Plans

Our directors and officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell ordinary shares on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer generally may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may generally buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information, subject to compliance with the terms of our insider trading policy.

Compensation Committee Interlocks and Insider Participation

During 2019, the members of our compensation committee were Ronald M. Hunt (Chairman), Mark Chin, Paul R. Edick (to June 2019), James I. Healy, M.D., Ph.D., and Shahzad Malik, M.D. No member of our compensation committee is, or has ever been, an officer or employee of our Company. None of our executive officers serve, or have served during the last year, as a member of the board of directors, compensation committee, or other board committee performing equivalent functions of any other entity that has one or more executive officers serving as one of our directors or on our compensation committee.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters.

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of February 29, 2020 by:

(a) each person, or group of affiliated persons, known by us to beneficially own more than 5% of our ordinary shares;

(b) each of our named executive officers;

(c) each of our directors; and

(d) all of our executive officers and directors as a group.

Beneficial ownership is determined according to the rules of the SEC and generally means that a person has beneficial ownership of a security if he, she, or it possesses sole or shared voting or investment power of that security, including share options that are exercisable within 60 days of February 29, 2020. Our ordinary shares issuable pursuant to share options are deemed outstanding for computing the percentage of the person holding such options and the percentage of any group of which the person is a member but are not deemed outstanding for computing the percentage of any other person. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons named in the table below have sole voting and investment power with respect to all ordinary shares shown that they beneficially own, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Section 13(d) and 13(g) of the Securities Act of 1933, as amended. Percentage ownership is based on 15,772,360 ordinary shares outstanding on February 29, 2020. Except as otherwise set forth below, the address of the beneficial owner is c/o Iterum Therapeutics plc, Block 2 Floor 3 Harcourt Centre, Harcourt Street, Dublin 2, Ireland.

	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
Principal Shareholders		
Entities affiliated with Advent Life Sciences[1]	868,161	5.8%
Entities affiliated with Arix Bioscience[2]	1,089,903	7.3%
Entities affiliated with Canaan Partners[3]	1,733,170	11.7%
Entities affiliated with Frazier Healthcare[4]	1,538,316	10.4%
Entities affiliated with New Leaf Ventures[5]	1,456,303	9.8%
Entities affiliated with Pivotal bioVenture Partners[6]	945,086	6.4%
Entities affiliated with Sofinnova Venture Partners[7]	1,726,514	11.6%
Directors and Named Executive Officers:		
Corey N. Fishman[8]	386,909	2.6%
Michael Dunne, MD[9]	237,732	1.6%
Judith M. Matthews[10]	83,990	*
Brenton K. Ahrens[11]	6,154	*
Mark Chin[2][12]	1,096,057	7.4%
Patrick J. Heron[4][13]	1,544,470	10.4%
Ronald M. Hunt[5][14]	1,467,544	9.9%
David G. Kelly[15]	28,445	*
Shahzad Malik, M.D.[1][16]	879,402	5.9%
All current executive officers and directors as a group (9 persons)[1][2][4][5][17]	5,730,703	37.8%

* less than 1%

(1) Consists of 868,161 shares reported as beneficially owned by Advent Life Sciences LLP, Advent Life Sciences Fund II LP and Shahzad Malik, M.D., of which each such reporting person reports sole voting power with respect to zero of these shares, shared voting power with respect to all 868,161 of these shares, sole dispositive power with respect to zero of these shares and shared dispositive power with respect to all 868,161 of these shares. Advent Life Sciences LLP is the general partner of Advent Life Sciences Fund II LP. Dr. Malik, a member of our board of directors, is a general partner of Advent Life Sciences LLP. The address for each of the reporting persons is 158-160 North Gower Street, London, NW1 2ND, United Kingdom. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13D/A that was filed with the SEC on January 29, 2020.

(2) Consists of 1,089,903 shares beneficially owned by Arix Bioscience Plc, Arix Bioscience Holdings Limited and Mark Chin, of which each such reporting person reports sole voting power with respect to zero of these shares, shared voting power with respect to all 1,089,903 of these shares, sole dispositive power with respect to zero of these shares and shared dispositive power with respect to all 1,089,903 of these shares. The shares are held directly by Arix Bioscience Holdings Limited. Mr. Chin, a member of our board of directors, is an investment director of Arix Bioscience Plc, which is the sole owner and parent of Arix Bioscience Holdings Limited. The address for each of the reporting persons is 20 Berkeley Square, Mayfair, London W1J 6EQ, United Kingdom. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13D/A that was filed with the SEC on January 27, 2020.

(3) Consists of 1,733,170 shares reported as beneficially owned by Canaan X L.P. and Canaan Partners X LLC, of which each such entity reports sole voting power with respect to 1,733,170 shares, shared voting power with respect to zero shares, sole dispositive power with respect to 1,733,170 shares and shared dispositive power with respect to zero shares. The shares are directly held by Canaan X L.P. Canaan Partners X LLC is the general partner of Canaan X L.P. and may be deemed to beneficially own the shares held by Canaan X L.P. Brenton K. Ahrens, Stephen M. Bloch, Daniel T. Ciporin, Wende S. Hutton, Maha S. Ibrahim, Deepak Kamra, Nina Kjellson, Guy M. Russo, Timothy Shannon and Hrach Simonian are the managing members of Canaan Partners X LLC. Investment, voting and dispositive decisions with respect to the shares held by Canaan X L.P. are made by the managers of Canaan Partners X LLC, collectively. Mr. Ahrens, a member of our board of directors, is a managing member of Canaan Partners X LLC. No manager or member of Canaan Partners X LLC has beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act) of any shares held by Canaan X L.P. The address for each of the reporting persons is 285 Riverside Avenue, Suite 250, Westport, Connecticut 06880. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13G that was filed with the SEC on February 6, 2019.

(4) Consists of (a) 1,197,161 shares reported as beneficially owned by Frazier Healthcare VII, L.P., of which such entity reports sole voting power with respect to zero shares, shared voting power with respect to 1,197,161 shares, sole dispositive power with respect to zero shares and shared dispositive power with respect to 1,197,161 shares, and (b) 341,155 shares held directly by Frazier Healthcare VII-A, L.P. of which such entity reports sole voting power with respect to zero shares, shared voting power with respect to 341,155 shares, sole dispositive power with respect to zero shares and shared dispositive power with respect to 341,155 shares. The general partner of Frazier Healthcare VII, L.P. and Frazier Healthcare VII-A, L.P. is FHM VII, L.P., a Delaware limited partnership, and the general partner of FHM VII, L.P. is FHM VII, L.L.C., a Delaware limited liability company, each of which are reported as the beneficial owner of 1,538,316 shares, of which each such entity reports sole voting power with respect to zero shares, shared voting power with respect to 1,538,316 shares, sole dispositive power with respect to zero shares and shared dispositive power with respect to 1,538,316 shares. Mr. Heron, a member of our board of directors, Alan Frazier, Nader Naini, Nathan Every, Brian Morfitt, and James Topper are members of FHM VII, L.L.C. and may be deemed to share voting and investment power with respect to the shares held by FHM VII, L.L.C. The address for each of the reporting persons is c/o Frazier Healthcare Partners, 601 Union Street, Suite 3200, Seattle WA 98101. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13D/A that was filed with the SEC on January 27, 2020.

(5) Consists of (a) 1,071,688 shares reported as beneficially owned by New Leaf Venture III, L.P. ("NLV-III"), New Leaf Venture Associates III, L.P. ("NLVA-III LP") and New Leaf Venture Management III, L.L.C. ("NLVM-III LLC"), of which each such entity reports sole voting power with respect to 1,071,688 shares, shared voting power with respect to zero shares, sole dispositive power with respect to 1,071,688 shares and shared dispositive power with respect to zero shares, and (b) 384,615 shares held by New Leaf Biopharma Opportunities II, L.P. ("NBPO-II"), New Leaf BPO Associates II, L.P. ("NBPO-IIA") and New Leaf BPO Management II, L.L.C. ("NBPO-IIM"), of which each such entity reports sole voting power with respect to 384,615 shares, shared voting power with respect to zero shares, sole dispositive power with respect to 384,615 shares and shared dispositive power with respect to zero shares. NLVA-III LP is the general partner of NLV-III and NLVM-III LLC is the general partner of NLVA-III LP. NBPO-IIA is the general partner of NBPO-II and NBPO-IIM is the general partner of NBPO-IIA. Mr. Hunt, a member of our board of directors and Vijay K. Lathi are individual managers of NLVM-III LLC and individual managers of NPBO-IIM, and as a result may be deemed to have shared power to vote and dispose of these shares. The address for each of the reporting persons other

than Vijay K. Lathi is c/o New Leaf Venture Partners, 420 Lexington Avenue, Suite 408, New York, NY 10170. The address for Vijay K. Lathi is c/o New Leaf Venture Partners, 2730 Sand Hill Road, Suite 110, Menlo Park, CA 94025. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13D/A that was filed with the SEC on January 27, 2020.

(6) Consists of 945,086 shares reported as beneficially owned by Pivotal bioVenture Partners Fund I, L.P., Pivotal bioVenture Partners Fund I G.P., L.P. and Pivotal bioVenture Partners Fund I U.G.P., Ltd., of which each such entity reports sole voting power with respect to zero shares, shared voting power with respect to 945,086 shares, sole dispositive power with respect to zero shares and shared dispositive power with respect to 945,086 shares. The shares are held directly by Pivotal bioVenture Partners Fund I, L.P. Pivotal bioVenture Partners Fund I G.P., L.P. is the general partner of Pivotal bioVenture Partners Fund I, L.P. and Pivotal bioVenture Partners Fund I U.G.P., Ltd is the general partner of Pivotal bioVenture Partners Fund I, G.P., L.P. The board of directors of Pivotal bioVenture Partners Fund I U.G.P., Ltd retains ultimate voting and investment control and power over the shares owned by Pivotal bioVenture Partners Fund I, L.P. The address for each of the reporting persons is 1700 Owens Street, Suite 595, San Francisco, CA 94158. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13G that was filed with the SEC on December 24, 2018.

(7) Consists of 1,726,514 shares reported as beneficially owned by Sofinnova Venture Partners IX, L.P. ("SVP IX"), Sofinnova Management IX, L.L.C. ("SM IX"), Dr. Michael F. Powell and Dr. James I. Healy, with respect to which SVP IX and SM IX report sole voting power and sole dispositive power, and Dr. Michael F. Powell and Dr. James I. Healy report shared voting power and shared dispositive power. SM IX is the general partner of SVP IX. Each of Dr. Healy and Michael Powell is a managing member of SM IX. The address for each of the reporting persons is c/o Sofinnova Ventures, 3000 Sand Hill Road, Bldg. 4, Suite 250, Menlo Park, CA 94025. We obtained the information regarding beneficial ownership of these shares solely from Schedule 13D/A that was filed with the SEC on January 24, 2020.

(8) Consists of (a) 239,953 shares held directly by Mr. Fishman, and (b) 146,956 shares issuable to Mr. Fishman pursuant to share options exercisable within 60 days of February 29, 2020.

(9) Consists of (a) 147,958 shares held directly by Dr. Dunne, and (b) 89,774 shares issuable to Dr. Dunne pursuant to share options exercisable within 60 days of February 29, 2020.

(10) Consists of (a) 56,130 shares held directly by Ms. Matthews, and (b) 27,860 shares issuable to Ms. Matthews pursuant to share options exercisable within 60 days of February 29, 2020.

(11) Consists of 6,154 shares beneficially owned by Mr. Ahrens.

(12) Includes 6,154 shares beneficially owned by Mr. Chin.

(13) Includes 6,154 shares held directly by Mr. Heron.

(14) Includes 11,241 shares issuable to Mr. Hunt pursuant to share options exercisable within 60 days of February 29, 2020.

(15) Consists of (a) 25,702 shares beneficially owned by Mr. Kelly and (b) 2,743 shares issuable to Mr. Kelly pursuant to share options exercisable within 60 days of February 29, 2020.

(16) Includes 11,241 shares issuable to Dr. Malik pursuant to share options exercisable within 60 days of February 29, 2020.

(17) Includes (a) 488,205 shares held by the current directors and executive officers, (b) 289,815 shares issuable to the current directors and executive officers pursuant to share options exercisable within 60 days of February 29, 2020.

Equity Compensation Plan Information

The following table provides certain aggregage information with respect to all of our equity compensation plans in effect as of December 31, 2019. As of December 31, 2019, we had two equity compensation plans, the 2018 Equity Incentive Plan, or the 2018 Plan, and the 2015 Equity Incentive Plan, or the 2015 Plan, each of which were approved by our shareholders.

Plan category	Number of securities to be issued upon exercise of outstanding options(1)	Weighted average exercise price of outstanding options(2)	Number of securities remaining for future issuance under equity compensation plan (excluding securities reflected in column (a))(3)
Equity compensation plans approved by shareholders	1,231,637	$7.92	537,631
Equity compensation plans not approved by shareholders	—	—	—
Total	1,231,637	$7.92	537,631

(1) This amount includes 31,367 shares subject to outstanding RSUs and 50,000 shares subject to oustanding PSUs, in each case as of December 31, 2019.

(2) The weighted-average exercise price is calculated based solely on the exercise prices of the outstanding options and does not reflect the shares that will be issued upon the vesting of outstanding RSUs and PSUs, which have no exercise price.

(3) The amount disclosed does not reflect an additional 594,758 ordinary shares authorized for issuance under the 2018 Plan as of February 14, 2020, as an annual increase in accordance with the terms of such plan.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The following is a description of transactions since January 1, 2018, to which we have been a party, in which the amount involved exceeds $120,000, and in which any of our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest. We refer to such transactions as "related party transactions" and such persons as "related parties." With the approval of our board of directors, we have engaged in the related party transactions described below. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, from unaffiliated third parties.

Participation in our Initial Public Offering

In May 2018, in our initial public offering, we issued an aggregate of 6,350,000 ordinary shares at a purchase price of $13.00 per share, which included 200,000 ordinary shares issued upon the exercise by the underwriters of their option to purchase additional shares. Certain of our existing shareholders and their affiliated entities, including affiliates of our directors, purchased an aggregate of approximately $42.9 million of our ordinary shares in our initial public offering at the initial public offering price. The table below sets forth the aggregate number of ordinary shares issued to our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, at the time of the transaction:

Name	Shares	Aggregate Purchase Price
Frazier Healthcare VII, L.P.	354,949	$ 4,614,337
Frazier Healthcare VII-A, L.P.	101,150	1,314,950
New Leaf Ventures III, L.P.	278,062	3,614,806
New Leaf Biopharma Opportunities II, L.P.	384,615	4,999,995
Canaan X, L.P.	506,656	6,586,528
Sofinnova Venture Partners IX, L.P.	500,000	6,500,000
Arix Bioscience Holdings Ltd.	337,606	4,388,878
Pivotal bioVenture Partners Fund I, L.P.	313,908	4,080,804
Domain Partners IX, L.P.	153,846	1,999,998
Advent Life Sciences LLP	8,144	105,872
Advent Life Sciences Fund II LP	228,840	2,974,920
Bay City Capital GF Xinde International Life Sciences USD Fund, L.P.	125,563	1,632,319
Corey Fishman	3,000	39,000
Michael Dunne	2,000	26,000
Judith M. Matthews	4,000	52,000
Total	3,302,339	$ 42,930,407

(1) Mr. Heron, a member of our board of directors, is a general partner of Frazier Healthcare Partners
(2) Mr. Hunt, a member of our board of directors, is a managing partner of New Leaf Venture Partners
(3) Mr. Ahrens, a member of our board of directors, is a general partner of Canaan.
(4) Dr. Healy, a former member of our board of directors, is a general partner of Sofinnova Ventures
(5) Mr. Chin, a member of our board of directors, is an investment director of Arix Bioscience
(6) Dr. Hopfner, a former member of our board, is a managing partner of Pivotal bioVenture Partners
(7) Dr. Malik, a member of our board of directors, is a general partner of Advent Life Sciences

Participation in Private Placement

On January 16, 2020, we entered into a Securities Purchase Agreement by and among us, Iterum Therapeutics Bermuda Limited (Iterum Bermuda), Iterum Therapeutics International Limited, Iterum Therapeutics US Limited and Iterum Therapeutics US Holding Limited (collectively, the Guarantors) and a limited number of accredited investors (the Purchasers) pursuant to which Iterum Bermuda sold and issued units consisting of (i) 6.500% Exchangeable Senior Subordinated Notes due 2025 (the Exchangeable Notes), fully and unconditionally guaranteed on an unsecured senior subordinated basis by the Guarantors, and (ii) Limited Recourse Royalty-Linked Subordinated Notes, fully and unconditionally guaranteed on an unsecured senior subordinated basis by the Guarantors (RLNs, and together with the Exchangeable Notes, the Units), to the Purchasers in a private placement (Private Placement). Certain of our existing shareholders and their affiliated entities, including affiliates of our directors, purchased an aggregate of 13,398 Units. The

table below sets forth the aggregate number of Units issued to our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, at the time of the transaction:

Name	Shares	Aggregate Purchase Price
Advent Life Sciences LLP	53	$ 53,000
Advent Life Sciences Fund II LP	1,495	1,495,000
Arix Bioscience Holdings Limited	1,900	1,900,000
Canaan X, L.P.	2,000	2,000,000
Frazier Healthcare VII, L.P.	1,167	1,167,000
Frazier Healthcare VII-A, L.P.	333	333,000
New Leaf Ventures III, L.P.	2,208	2,208,000
New Leaf Biopharma Opportunities II, L.P.	792	792,000
Sofinnova Venture Partners IX, L.P.	1,750	1,750,000
Domain Partners IX, L.P.	1,000	1,000,000
Pivotal bioVenture Partners Fund I, LP	700	700,000
Total	13,398	$ 13,398,000

In connection with the Private Placement, we also entered into an investor rights agreement (the 2020 Investor Rights Agreement) with the Purchasers (including certain of our directors and holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, as listed above) pursuant to which Iterum Bermuda and the Guarantors agreed to file a registration statement covering (a) in the case of a registration statement on Form S-1, the resale of the Exchangeable Notes, the ordinary shares issuable in connection with the exchange of the Exchangeable Notes (the Exchange Shares) and the RLNs or (b) in the case of a registration statement on Form S-3, the Exchange Shares (the securities in (a) and (b) together, the Registrable Securities). Under the 2020 Investor Rights Agreement, we agreed to file an initial registration statement covering the resale by the Purchasers of their Registrable Securities within 10 business days following the later of (x) the earlier of (I) the consummation of an offering of subscription rights to purchase additional Securities that we agreed to undertake in connection with the Private Placement and (II) January 21, 2021 and (y) the date on which the number of our unissued ordinary shares available for issuance (less certain reserved shares) is greater than the total number of ordinary shares issuable upon exchange of the then outstanding Exchangeable Notes. If a registration statement has not been filed within the timeframe set forth in the 2020 Investor Rights Agreement or the registration statement covering the Registrable Securities ceases to be effective for resales of Registrable Securities for more than 60 consecutive days or for more than 120 days in any 12-month period, then, subject to the terms of the 2020 Investor Rights Agreement, additional interest will accrue on the Exchangeable Notes and the RLNs.

In addition, pursuant to the terms of the 2020 Investor Rights Agreement, for so long as Sarissa Capital Management LP (Sarissa) and its affiliates own at least 5% or 12.5%, as applicable, of our outstanding ordinary shares on a fully diluted basis, promptly, and in any event no more than 5 business days following written request of Sarissa, we will cause our board of directors to increase to consist of nine or 10 members, as applicable, and we will cause the board of directors to consist of no more than 10 members without the prior written consent of Sarissa. In addition, for so long as Sarissa and its affiliates own at least 12.5% of our outstanding ordinary shares on a fully diluted basis, Sarissa will have the right to designate two directors to our board of directors and, for so long as Sarissa and its affiliates own at least 5% but less than 12.5%, it will have the right to designate one director to our board of directors (Investor Designees). Pursuant to the terms of the 2020 Investor Rights Agreement, such Investor Designees will be appointed to our board of directors and to be members of the class of directors that was subject to reelection at our most recent annual meeting of shareholders. The Investor Designees will be entitled to be a member of any committee of our board of directors subject to the terms of the 2020 Investor Rights Agreement. Pursuant to the terms of the 2020 Investor Rights Agreement, the purchasers party thereto, subject to specified exceptions, have agree with us to vote in favor of the election of the Investor Designees, and we have agreed to cause the Investor Designees to be named in any relevant proxy statement..

Furthermore, pursuant to the terms of the 2020 Investor Rights Agreement, for so long as Sarissa owns 10% of our outstanding ordinary shares on a fully diluted basis, Sarissa will have a right of first offer with respect to future proposed equity financings of ours up to that portion of such new securities which equals Sarissa's percentage ownership of our outstanding ordinary shares on a fully diluted basis, subject to specified exceptions for certain exempt issuances and pursuant to specified procedures. In the event our board of directors determines in good faith that we must conduct an equity financing on an expedited basis without compliance with the right of first offer described above in order to avoid material harm to us or any of our affiliates, we may effect and consummate such equity financing and, as promptly as practicable following the consummation of such equity financing, Sarissa will have the opportunity to participate in such equity financing and be put in the same place (including in respect of the percentage ownership of our equity securities) Sarissa would have been had such equity financing been effected in accordance with the terms of the right of first offer. As set forth in the 2020 Investor Rights Agreement, in any 12 month period, we may conduct an equity financing without compliance with the pre-emptive rights described above (an Excused Issuance); provided that we may not issue new securities (other than specified exempted securities) exceeding (in the aggregate with all other Excused Issuances during such 12 month period) 5% of our issued and outstanding ordinary shares on a fully diluted basis, and we may not issue new securities (other than specified exempted securities) in exchange for consideration (whether in cash or other property) the value of which exceeds (in the aggregate with all other Excused Issuances during such 12 month period) $5.0 million. We may only consummate two Excused Issuances for so long as the 2020 Investor Rights Agreement is in effect.

2017 Investor Rights Agreement

In May 2017, we entered into an amended and restated investor rights agreement with holders of our preferred shares and ordinary shares, including certain holders of more than 5% of our share capital, our executive officers, certain of our directors, and entities affiliated with certain of our directors (the 2017 Investor Rights Agreement). Since the closing of our initial public offering, those holders are entitled to certain registration rights, including the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. The 2017 Investor Rights Agreement also gave the shareholders that are parties thereto the right to participate in new issuances of equity securities by us, subject to certain exceptions. This right to participate in new issuances of equity securities terminated by its terms upon the completion of our initial public offering in May 2018.

Amended Offer Letters

In May 2018 we entered into amended offer letters with certain of our executive officers. For more information regarding these amended offer letters, see *Item 11. Executive Compensation — Employment Agreements with Executive Officers* above.

Equity Grants

We have granted stock option and RSU awards to certain non-employee members of our board of directors. For details and a description of these awards, see *Item 11. Executive Compensation* above.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. In addition, our subsidiary, Iterum Therapeutics US Limited, has entered into an indemnification agreement with each of our directors and executive officers. These agreements, among other things, require us to indemnify an indemnitee to the fullest extent permitted by applicable law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the indemnitee in any action or proceeding, including any action or proceeding by us or in our right, arising out of the person's services as a director or executive officer. We also maintain a directors and officers liability insurance policy which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

Related Party Transaction Policy

We have adopted a formal written policy that our executive officers, directors, key employees, holders of more than 5% of any class of our voting securities, and any member of the immediate family of and any entity affiliated with any of the foregoing persons, are not permitted to enter into a related-party transaction with us without the prior consent of our audit committee, or other independent body of our board of directors in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest. Any request for us to enter into a transaction with an executive officer, director, principal shareholder, or any of their immediate family members or affiliates, in which the amount involved exceeds $120,000, is required to first be presented to our audit committee for review, consideration, and approval. In approving or rejecting any such proposal, our audit committee will consider the relevant facts and circumstances available and deemed relevant to our audit committee, including, but not limited to, whether the transaction will be on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related party's interest in the transaction.

Some of the transactions described in this section were entered into prior to the adoption of this policy. Although we did not have a written policy for the review and approval of transactions with related persons prior to May 2018, our board of directors has historically reviewed and approved any transaction where a director or officer had a financial interest, including the relevant transactions described above. Prior to approving such a transaction, the material facts as to a director's or officer's relationship or interest in the agreement or transaction were disclosed to our board of directors. Our board of directors took this information into account when evaluating the transaction and in determining whether such transaction was fair to us and in the best interest of all our shareholders.

Director independence

Applicable rules of The Nasdaq Stock Market, or Nasdaq, require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq rules require that within one year of the date of the completion of an initial public offering, all the members of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

In order to be considered independent for purposes of Rule 10A-3 under the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

In order to be considered independent for purposes of Rule 10C-1 under the Exchange Act, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including

any consulting, advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In March 2020, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that none of Mr. Ahrens, Mr. Chin, Mr. Heron, Mr. Hunt, Mr. Kelly or Dr. Malik, representing six of our seven current directors, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under Rule 5605(a)(2) of the Nasdaq Marketplace Rules. Mr. Fishman is not an independent director under Rule 5605(a)(2) because he is our President and Chief Executive Officer. Our board of directors has also determined that Messrs. Kelly, Ahrens and Chin, who comprise our audit committee, Messrs. Hunt and Chin and Dr. Malik, who comprise our compensation committee, and Messrs. Heron, Hunt and Kelly and Dr. Malik, who comprise our nominating and corporate governance committee, satisfy the independence standards for such committees established by the SEC and Nasdaq. In making such determination, our board of directors considered the relationships that each such non-employee director has with our Company, including the transactions described in this Item 13, and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our shares by each non-employee director as described above Item 12.

Item 14. Principal Accounting Fees and Services.

The following table presents fees for professional audit services and other services rendered by KPMG to us for the fiscal years ended December 31, 2019 and 2018:

	Year Ended December 31, 2019	Year Ended December 31, 2018
Audit fees (1)	$235,251	$380,070
Audit related fees (2)	—	—
Tax fees (3)	110,758	80,235
All other fees	—	—
	$346,009	$460,305

(1) "Audit Fees" consist of fees billed for professional services performed by KPMG for the audit of our annual financial statements, the review of interim financial statements, and related services that are normally provided in connection with our initial public offering and registration statements on Form S-3 and Form S-8. Included in the 2018 audit fees is $208,427 of fees billed in connection with our initial public offering in May 2018.
(2) "Audit related fees" consist of fees billed by an independent registered public accounting firm for assurance and related services that are reasonably related to the performance of the audit or review of our consolidated financial statements.
(3) "Tax fees" consist of fees for professional services, including tax consulting and compliance performed by an independent registered public accounting firm.

All of these services were pre-approved by the audit committee in accordance with the "*Policy on Audit Committee Pre-Approval of Services*" described below. No work carried out in connection with the audit of our financial statements was performed by persons other than KPMG's full time, permanent employees.

Policy on Audit Committee Pre-Approval of Services

Consistent with SEC policies regarding auditor independence, the audit committee has responsibility for appointing, setting compensation and overseeing the work of our independent registered public accounting firm. In recognition of this responsibility, the audit committee reviews and pre-approves all audit and permissible non-audit services provided by our independent registered public accounting firm; provided, however, that de minimis non-audit services may instead be approved in accordance with applicable SEC rules.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) Consolidated Financial Statements

See Index to Consolidated Financial Statements at Item 8 herein.

(2) Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the consolidated financial statements or notes thereto.

(3) Exhibits

The following is a list of exhibits filed or furnished as part of this Annual Report on Form 10-K;

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
3.1	Constitution of Iterum Therapeutics plc		Form 8-K (Exhibit 3.1)	May 30, 2018	001-38503
4.1	Form of Ordinary Share Certificate of Registrant.		Form S-1 (Exhibit 4.1)	May 1, 2018	333-224582
4.2	Indenture (including form of note), dated January 21, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and U.S. Bank National Association, as trustee.	X			
4.3	Form of 6.500% Exchangeable Senior Subordinated Note due 2025 (included within Exhibit 4.2).	X			
4.4	Indenture (including form of note), dated January 21, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited, Iterum Holders' Representative LLC and Computershare Trust Company, N.A., as trustee.	X			
4.5	Form of Limited Recourse Royalty-Linked Subordinated Note (included within Exhibit 4.4).	X			
4.6	Description of the registrant's registered securities.	X			
10.1†	License Agreement by and among Registrant, Iterum Therapeutics International Limited and Pfizer Inc. dated as of November 18, 2015.		Form S-1 (Exhibit 10.1)	May 1, 2018	333-224582
10.2	Amended and Restated Investor Rights Agreement by and between Registrant and certain of its shareholders dated May 18, 2017.		Form S-1 (Exhibit 10.2)	May 1, 2018	333-224582
10.3+	2015 Equity Incentive Plan.		Form S-1 (Exhibit 10.3)	May 1, 2018	333-224582
10.4+	Forms of U.S. Stock Option Agreement, Stock Option Grant Notice and Notice of Exercise under the 2015 Equity Incentive Plan.		Form S-1 (Exhibit 10.4)	May 1, 2018	333-224582
10.5+	Forms of Irish Stock Option Agreement, Stock Option Grant Notice and Notice of Exercise under the 2015 Equity Incentive Plan.		Form S-1 (Exhibit 10.5)	May 1, 2018	333-224582
10.6+	2018 Equity Incentive Plan.		Form S-1/A (Exhibit 10.6)	May 16, 2018	333-224582
10.7+	Forms of U.S. Stock Option Terms and Conditions and Stock Option Grant Notice under the 2018 Equity Incentive Plan.		Form S-1 (Exhibit 10.7)	May 1, 2018	333-224582
10.8+	Forms of International Stock Option Terms and Conditions and Stock Option Grant Notice under the 2018 Equity Incentive Plan.		Form S-1 (Exhibit 10.8)	May 1, 2018	333-224582
10.9+	Form of Restricted Share Unit Award Agreement under the 2018 Equity Incentive Plan.		Form S-1 (Exhibit 10.9)	May 1, 2018	333-224582
10.10+	Form of 2020 Restricted Share Unit Award Agreement under the 2018 Equity Incentive Plan.	X			
10.12	Form of Indemnity Agreement by and between the Registrant and its directors and officers.		Form S-1 (Exhibit 10.10)	May 1, 2018	333-224582
10.12	Form of Indemnity Agreement by and between Iterum Therapeutics US Limited and its directors and officers.		Form S-1 (Exhibit 10.11)	May 1, 2018	333-224582
10.13+	Employment Terms by and between Iterum Therapeutics US Limited and Corey N. Fishman dated November 18, 2015.		Form S-1 (Exhibit 10.12)	May 1, 2018	333-224582

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
10.14+	Amendment to Employment Agreement by and between Iterum Therapeutics US Limited and Corey N. Fishman dated May 2, 2018.		Form S-1/A (Exhibit 10.13)	May 4, 2018	333-224582
10.15+	Employment Terms by and between Iterum Therapeutics US Limited and Michael W. Dunne dated November 18, 2015.		Form S-1 (Exhibit 10.14)	May 1, 2018	333-224582
10.16+	Employment Terms by and between Iterum Therapeutics US Limited and Judith M. Matthews dated November 18, 2015.		Form S-1 (Exhibit 10.15)	May 1, 2018	333-224582
10.17+	Amendment to Employment Agreement by and between Iterum Therapeutics US Limited and Judith M. Matthews dated May 2, 2018.		Form S-1/A (Exhibit 10.16)	May 4, 2018	333-224582
10.18+	Non-Employee Director Compensation Policy.		Form S-1/A (Exhibit 10.18)	May 16, 2018	333-224582
10.19	Loan and Security Agreement by and among Silicon Valley Bank, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited, and Iterum Therapeutics US Limited, dated April 27, 2018.		Form S-1/A (Exhibit 10.19)	May 4, 2018	333-224582
10.20	Intellectual Property Security Agreement by and among Silicon Valley Bank, the Registrant, Iterum Therapeutics International Limited, Iterum Therapeutics US Holding Limited, and Iterum Therapeutics US Limited, dated April 27, 2018.		Form S-1/A (Exhibit 10.20)	May 4, 2018	333-224582
10.21	Warrant to Subscribe for Shares, issued to Silicon Valley Bank, dated April 27, 2018.		Form S-1/A (Exhibit 10.21)	May 4, 2018	333-224582
10.22	Warrant to Subscribe for Shares, issued to Life Sciences Fund II LLC, dated April 27, 2018.		Form S-1/A (Exhibit 10.22)	May 4, 2018	333-224582
10.23	Additional Form of Warrant to Subscribe for Ordinary Shares as may be issued to Silicon Valley Bank pursuant to the Loan and Security Agreement.		Form S-1/A (Exhibit 10.23)	May 4, 2018	333-224582
10.24	Additional Form of Warrant to Subscribe for Ordinary Shares as may be issued to Life Sciences Fund II LLC pursuant to the Loan and Security Agreement.		Form S-1/A (Exhibit 10.24)	May 4, 2018	333-224582
10.25	Securities Purchase Agreement, dated as of January 16, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and the Investors party thereto.		Form 8-K (Exhibit 10.1)	January 17, 2020	001-38503
10.26	Investor Rights Agreement, dated January 21, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics plc, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and the Investors party thereto.	X			
10.27	First Amendment to Loan and Security Agreement, dated as of January 16, 2020, by and among Iterum Therapeutics Bermuda Limited, Iterum Therapeutics International Limited, Iterum Therapeutics US Limited, Iterum Therapeutics US Holding Limited and Silicon Valley Bank.		Form 8-K (Exhibit 10.3)	January 17, 2020	001-38503
21.1	Subsidiaries of the Registrant.	X			
23.1	Consent of KPMG, Independent Registered Public Accounting Firm.	X			

Exhibit No.	Description of Document	Filed with this report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File Number
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X			
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X			
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X			

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+	Indicates management contract or compensatory plan.
†	Confidential treatment has been requested for certain provisions omitted from this Exhibit pursuant to Rule 406 promulgated under the Securities Act. The omitted information has been filed separately with the Securities and Exchange Commission.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

ITERUM THERAPEUTICS PLC

Date: March 12, 2020

By: /s/ Corey N. Fishman
Corey N. Fishman
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ Corey N. Fishman Corey N. Fishman	President and Chief Executive Officer (Principal Executive Officer)	March 12, 2020
/s/ Judith M. Matthews Judith M. Matthews	Chief Financial Officer (Principal Financial and Accounting Officer)	March 12, 2020
/s/ Brenton K. Ahrens Brenton K. Ahrens	Director	March 12, 2020
/s/ Mark Chin Mark Chin	Director	March 12, 2020
/s/ Patrick J. Heron Patrick J. Heron	Director	March 12, 2020
/s/ Ronald M. Hunt Ronald M. Hunt	Director	March 12, 2020
/s/ David G. Kelly David G. Kelly	Director	March 12, 2020
/s/ Shahzad Malik Shahzad Malik, M.D.	Director	March 12, 2020