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, 2018

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: 001-38670

Entasis Therapeutics Holdings Inc.

(Exact name of Registrant as specified in its charter)

Delaware	2834	82-4592913
(State or Other Jurisdiction of Incorporation or Organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

35 Gatehouse Drive
Waltham, MA 02451
(781) 810-0120

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

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

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value $0.001 per share	Nasdaq Global Market

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 Securities 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 the 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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

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 Exchange Act.) Yes ☐ No ☒

There was no aggregate market value of shares of common stock held by non-affiliates of the registrant as of June 30, 2018, the last business day of the registrant's most recently completed second fiscal quarter, because the registrant's common stock was not trading on any exchange on that date.

As of March 25, 2019, there were 13,127,128 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2019 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2018, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or Exchange Act. All statements other than statements of historical fact are "forward-looking statements" for purposes of this Annual Report on Form 10-K. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "could," "estimate," "expects," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative or plural of those terms, and similar expressions.

Forward-looking statements include, but are not limited to, statements about:

- our plans to develop and commercialize our product candidates;
- our planned clinical trials for our product candidates;
- the timing of the availability of data from our clinical trials;
- the timing of our selection of an initial clinical candidate from our NBP program;
- our expectation that the efficacy and safety data from our planned Phase 3 trials, if positive, will be sufficient to support submission of an NDA to the FDA;
- our ability to obtain grants or other government funding to develop our product candidates;
- our ability to take advantage of benefits offered by current and pending legislation related to the development of products addressing antimicrobial resistance;
- the timing of our planned regulatory filings;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the clinical utility of our product candidates and their potential advantages compared to other treatments;
- our commercialization, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for the manufacture of our product candidates;
- our ability to establish and maintain collaborations and to recognize the potential benefits of such collaborations;
- our estimates regarding the market opportunities for our product candidates;
- our intellectual property position and the duration of our patent rights; and
- our estimates regarding future expenses, capital requirements and needs for additional financing.

Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part I, Item 1A, "Risk Factors," herein and for the reasons described elsewhere in this Annual Report on Form 10-K. Any forward-looking statement in this Annual Report on Form 10-K reflects our current view with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not rely on these 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 future results, levels of activity, performance or achievements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained these industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources and we have not independently verified the data from third-party sources. In some cases, we do not expressly refer to the sources from which these data are derived.

In addition, assumptions and estimates of our and our industry's future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled "Risk Factors." These and other factors could cause our future performance to differ materially from our assumptions and estimates.

In this Annual Report on Form 10-K, unless otherwise stated or as the context otherwise requires, references to "Entasis," "the Company," "we," "us," "our" and similar references refer to Entasis Therapeutics Holdings Inc. and its wholly owned subsidiaries. This Annual Report on Form 10-K also contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

PART I

Item 1. BUSINESS

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel antibacterial products to treat serious infections caused by multidrug-resistant Gram-negative bacteria. Leveraging our targeted-design platform, we have engineered and developed product candidates that target clinically validated mechanisms to address antibiotic resistance. Our lead product candidate, ETX2514, as well as one of our other product candidates, ETX0282, inhibit one of the most prevalent forms of bacterial resistance, β-lactamase enzymes, so named because of their ability to inactivate β-lactam antibiotics, one of the most commonly used classes of antibiotics. By blocking this resistance mechanism, these product candidates, when administered in combination with β-lactam antibiotics, are designed to restore the efficacy of those antibiotics. Our other product candidate, zoliflodacin, targets the validated mechanism of action of the fluoroquinolone class of antibiotics, but does so in a novel manner to avoid existing fluoroquinolone resistance.

ETX2514SUL is a fixed-dose combination of ETX2514, a novel broad-spectrum intravenous, or IV, β-lactamase inhibitor, or BLI, with sulbactam, an IV β-lactam antibiotic, that we are developing for the treatment of a variety of serious multidrug-resistant infections caused by *Acinetobacter baumannii*, or *Acinetobacter*. We have completed three separate Phase 1 clinical trials, including one evaluating the penetration of ETX2514SUL into the lung and one in renally impaired patients. In addition, we have completed a Phase 2 clinical trial in patients with complicated urinary tract infections, or UTIs. Based on a series of discussions with the U.S. Food and Drug Administration, or FDA, including an end-of-Phase-2 meeting, we are in the process of initiating a single Phase 3 clinical trial with data expected in the second half of 2020.

Zoliflodacin, is a novel orally administered molecule that inhibits bacterial gyrase, an essential enzyme in bacterial reproduction, for the treatment of drug-resistant Neisseria gonorrhoeae, the bacterial pathogen responsible for gonorrhea. Intramuscular ceftriaxone now represents the last-resort treatment option for gonorrhea, although resistant strains are beginning to emerge. We believe that there is a growing unmet need for an oral antibiotic that will reliably treat patients with gonorrhea, including multidrug-resistant gonorrhea. We have completed several Phase 1 clinical trials and a Phase 2 clinical trial of zoliflodacin in patients with uncomplicated gonorrhea. The results of the Phase 2 clinical trial were published in the New England Journal of Medicine in November 2018. We intend to initiate a Phase 3 clinical trial in mid-2019 with data expected in 2021. The Phase 3 clinical trial will be funded by our nonprofit collaborator, the Global Antibiotic Research and Development Partnership, or GARDP.

We are also developing ETX0282CPDP for the treatment of complicated UTIs, including those caused by extended-spectrum β-lactamase, or ESBL, -producing bacterial strains or carbapenem-resistant *Enterobacteriaceae*, or CRE. ETX0282CPDP is an oral, fixed-dose combination of ETX0282, a novel oral BLI, with cefpodoxime proxetil, an oral β-lactam antibiotic. We believe there is a significant unmet need for new oral antibiotics that reliably treat patients with multidrug-resistant Gram-negative infections. We initiated a multi-part Phase 1 clinical trial of ETX0282CPDP in Australia in the second quarter of 2018 and expect to receive data from the Phase 1 trial in mid-2019.

Our targeted-design platform was initially developed by AstraZeneca and its affiliates to address the limitations of traditional approaches to the research and development of novel antimicrobial agents. We acquired this platform as part of our spin-out from AstraZeneca AB in 2015 and our team has since used its significant experience in research and development at global pharmaceutical companies to further refine the platform. All our product candidates and our preclinical program have been developed using our targeted-design platform. We are also using our platform to develop a novel class of antibiotics, non β-lactam inhibitors of the penicillin-binding proteins, or NBPs. Penicillin-binding proteins, or PBPs, are clinically validated targets of β-lactam antibiotics, such as penicillins and carbapenems. Due to their differentiated chemical structure, our NBPs are not subject to inactivation by β-lactamases, unlike β-lactam antibiotics. Accordingly, we believe our NBPs constitute a potential new class of Gram-negative antibacterial agents with no pre-existing resistance that are designed to target a broad spectrum of pathogens, including *Pseudomonas aeruginosa*, or *Pseudomonas*. We expect to select an initial clinical candidate from our NBP program in 2019.

Antibiotic resistance is a growing global health threat and occurs when bacteria develop mechanisms to reduce or eliminate antibiotic effectiveness. When bacteria develop resistance to at least one drug in three or more antibiotic classes, they are commonly referred to as multidrug-resistant. Antibiotic-resistant infections often result in high morbidity and, in many cases, mortality. According to the Review on Antimicrobial Resistance, over 700,000 people worldwide die each year from antibiotic-resistant infections and up to 10 million lives per year could be at risk by 2050. In the United States alone, antibiotic-resistant infections are estimated to add $20 billion per year to healthcare costs. Due to the limitations of current treatment options and growing antibiotic resistance rates, the pathogens targeted by our current product candidates are all identified as high priority targets by the U.S. Centers for Disease Control and Prevention, or CDC, the World Health Organization and the Infectious Diseases Society of America.

Our Pipeline

The following table summarizes the status of our product candidates and preclinical program, which have all been developed using our targeted-design platform:

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Milestones	Commercial Rights	Partnerships
ETX2514SUL *IV*	Multi-drug resistant *Acinetobacter* infections					▪ Initiating Phase 3 trial; data expected 2H 2020	Worldwide excluding Asia-Pacific(1)	zai Lab
Zoliflodacin *Oral*	Uncomplicated gonorrhea					▪ Initiate Phase 3 trial in mid-2019	All developed countries(2)	GARDP, NIH
ETX0282CPDP *Oral*	Complicated UTIs (*Enterobacteriaceae* including ESBL-producing and CRE)					▪ Phase 1 data expected mid-2019	Worldwide	CARB-X
NBP Program *IV*	Gram-negative infections (initially multi-drug resistant *Pseudomonas*)					▪ Select initial clinical candidate in 2019	Worldwide	CARB-X

(1) Zai Lab (Shanghai) Co., Ltd. has licensed exclusive rights to ETX2514SUL in the Asia-Pacific region.

(2) GARDP will fully fund the Phase 3 development program for the treatment of uncomplicated gonorrhea. GARDP has commercial rights in low-income and specified middle-income countries. Entasis has retained commercial rights in all other countries, including the major markets in North America, Europe and Asia-Pacific.

Our Product Candidates

To address the problem of growing antibiotic resistance, we are developing a portfolio of novel product candidates, including:

ETX2514 in combination with sulbactam for the treatment of multidrug-resistant Acinetobacter infections

We are developing ETX2514 as a fixed-dose combination with sulbactam, which we refer to as ETX2514SUL, for the treatment of infections caused by multidrug-resistant *Acinetobacter. Acinetobacter* can cause severe pneumonia, as well as bloodstream, urinary tract and wound infections. Pneumonia and bloodstream infections caused by drug-resistant *Acinetobacter* can have mortality rates approaching 50%. Resistance rates of *Acinetobacter* to current standard-of-care treatments are some of the highest reported, between 50% and 60% in the United States and greater than 80% in

parts of Europe and Asia. There are four classes of β-lactamases, known as Classes A, B, C and D. *Acinetobacter* resistance to β-lactams is primarily driven by the expression of Class D β-lactamases, often in combination with Class A and/or Class C β-lactamases. To our knowledge, unlike currently marketed BLIs, ETX2514 is the first clinical-stage BLI with broad-spectrum activity across these three classes, most importantly Class D. We believe this broad coverage gives ETX2514 the potential to restore the efficacy of β-lactam antibiotics against *Acinetobacter*.

We selected sulbactam as the β-lactam antibiotic to combine with ETX2514 based on *in vitro* and *in vivo* analyses in which we observed sulbactam's superior microbiological potency compared to other β-lactam antibiotics we studied. Physicians have used sulbactam, either alone or in combination with ampicillin, to treat *Acinetobacter* infections; however, β-lactamase mediated resistance has rendered sulbactam largely ineffective. We believe ETX2514 effectively restores the activity of sulbactam against drug-resistant strains of *Acinetobacter*.

We have completed a four-part Phase 1 clinical trial in 124 healthy volunteers and a Phase 1 clinical trial evaluating penetration of ETX2514SUL into the lung in 30 healthy volunteers, where in both, ETX2514SUL was generally well tolerated. In addition, we have completed an additional Phase 1 clinical trial to assess pharmacokinetics in renally impaired patients, which has provided data to enable the development of a dose-adjustment protocol for patients with varying degrees of renal impairment.

To optimize our Phase 3 clinical trial, we completed a Phase 2 clinical trial in adult patients with complicated UTIs, including acute pyelonephritis (kidney infection) to provide additional safety and pharmacokinetic data. Eighty patients were randomized to receive either a dose of ETX2514SUL (ETX2514 1 g plus sulbactam 1 g) or placebo every six hours for seven days. Patients in both arms also received background therapy, which is current standard-of-care, with 500 mg of IMI administered through IV every six hours. ETX2514SUL was generally well tolerated. There were no serious adverse events reported and the adverse event profile of ETX2514SUL plus IMI, was similar to that of the IMI plus placebo comparator arm. Pharmacokinetic data observed in the Phase 2 trial was consistent with the pharmacokinetic data observed in the Phase 1 clinical trial in healthy volunteers. ETX2514SUL plus IMI showed similar microbiological success in the microbiologically evaluable population as placebo plus IMI (80% vs. 81%) and both treatment groups achieved 100% clinical success in the clinically evaluable population.

In an exploratory analysis of the Phase 2 clinical trial, we evaluated the efficacy of ETX2514SUL plus IMI against complicated UTIs caused by imipenem-non-susceptible pathogens. Eight patients had a complicated UTI caused by imipenem-non-susceptible pathogens (three in the treatment arm and five in the placebo arm). ETX2514SUL plus IMI eradicated isolates in all patients (100% [3/3]) compared to 60% (3/5) in patients receiving placebo plus IMI.

Based on a series of discussions with the FDA, including an end-of-Phase-2 meeting, we are in the process of initiating a single Phase 3 clinical trial of ETX2514SUL and expect to receive data from the trial in the second half of 2020. We believe the data from our Phase 1 and Phase 2 clinical trials, combined with the data from a single Phase 3 clinical trial, if positive, will be sufficient to support the submission of a new drug application, or NDA, to the FDA.

Throughout our clinical trials, we plan to collect data on the activity of ETX2514SUL in combination with IMI against a range of Gram-negative pathogens in addition to *Acinetobacter*. Based on the results of our preclinical studies and clinical trials, we believe that ETX2514 has the potential to restore the activity of imipenem against multiple bacterial pathogens, such as CRE and carbapenem-resistant *Pseudomonas*. We believe this may allow us to expand the clinical utility of ETX2514SUL.

In April 2018, we entered into a license and collaboration agreement with Zai Lab (Shanghai) Co., Ltd., or Zai Lab, pursuant to which Zai Lab licensed exclusive rights to ETX2514 and ETX2514SUL in the Asia-Pacific region. Under the terms of the agreement, Zai Lab will fund most of our clinical trial costs in China for ETX2514SUL, including all costs in China for our planned Phase 3 clinical trial of ETX2514SUL, apart from patient drug supply. Zai Lab will take the lead in China by conducting the screening, enrollment and treatment of patients, and will coordinate development, registration and commercialization of ETX2514SUL in China. See the section titled "Business—Commercial Agreements—License and Collaboration Agreement with Zai Lab" for additional information.

Zoliflodacin for the treatment of uncomplicated gonorrhea

We are developing zoliflodacin as an oral antibiotic monotherapy for the treatment of uncomplicated gonorrhea. Uncomplicated gonorrhea is *N. gonorrhoeae* infections of the urethra, cervix, pharynx or rectum, and are more common than complicated gonorrhea. *N. gonorrhoeae* is the bacterial pathogen responsible for gonorrhea, an extremely prevalent sexually transmitted disease that affects an estimated 78 million people worldwide each year. In the United States, the CDC estimates an annual incidence of 820,000 infections caused by *N. gonorrhoeae*. Ciprofloxacin and other oral fluoroquinolone antibiotics were widely used for the treatment of gonorrhea. Fluoroquinolones bind to and inhibit bacterial gyrase, an essential bacterial enzyme, effectively disrupting the process of DNA synthesis in the bacteria and its ability to reproduce. However, their widespread use led to mutations in the gyrase, which resulted in the emergence of fluoroquinolone resistance, making these antibiotics increasingly ineffective. As a result, fluoroquinolone antibiotics are rarely used to treat gonorrhea today in the United States and have been largely replaced by extended-spectrum cephalosporins, or ESCs. Intramuscular ceftriaxone, an ESC, now represents the last-resort treatment option for gonorrhea, although resistant strains are beginning to emerge. Cefixime, an ESC closely related to ceftriaxone, was the last oral monotherapy recommended for first-line treatment in the CDC's gonorrhea treatment guidelines, but the CDC removed it in 2012 after 0.1% of isolates exhibited resistance and 1.4% exhibited decreased susceptibility. This action was taken in part to delay the emergence of resistant strains of ceftriaxone and to prolong its effectiveness as a last-resort treatment. Historically, to reduce the risk of spreading drug-resistant pathogens in gonorrhea, the CDC has changed treatment guidelines when resistance rates to recommended first-line treatments reach 5%.

Like fluoroquinolones, zoliflodacin targets bacterial gyrase, but in a different manner to avoid existing fluoroquinolone resistance as well as ESC resistance. We have observed potent *in vitro* activity by zoliflodacin against *N. gonorrhoeae* strains, including those with high-level resistance to fluoroquinolones or to ESCs.

In our Phase 2 clinical trial, a single 3.0 g oral dose of zoliflodacin exhibited a 100% cure rate of urogenital and rectal gonorrhea in the per-protocol population. To our knowledge, zoliflodacin is the only novel treatment in active development with the potential to provide an oral alternative to intramuscular injections of ceftriaxone for the treatment of drug-resistant gonorrhea. If approved, we believe zoliflodacin has the potential to become the recommended first-line treatment of uncomplicated gonorrhea, especially as resistance to ceftriaxone increases. In addition, we believe patients would choose oral zoliflodacin over one or more intramuscular injections of ceftriaxone, which can be painful and require patient monitoring by a healthcare administrator.

We have entered into a collaboration with GARDP to co-develop zoliflodacin in a Phase 3 clinical trial. GARDP will fund all the Phase 3 development costs and will receive commercial rights for zoliflodacin in low-income and specified middle-income countries. We have retained commercial rights in all other countries, including the major markets in North America, Europe and Asia-Pacific. We anticipate initiating the Phase 3 clinical trial in mid-2019 with data expected in 2021.

ETX0282 in combination with cefpodoxime for the oral treatment of complicated UTIs

We are initially developing ETX0282 in combination with the β-lactam cefpodoxime proxetil, or cefpodoxime, which combination we refer to as ETX0282CPDP, for the oral treatment of complicated UTIs, including those caused by bacterial strains producing extended-spectrum β-lactamase, or ESBL, or by CRE. Oral antibiotics are commonly used in the community setting as first-line treatment for UTIs, which, if left unresolved, can have serious consequences, including life-threatening kidney infections. We believe that approximately 15 million UTIs occur annually in the United States, of which we estimate that 4.0 million are complicated. A complicated UTI is one associated with an underlying condition that increases the risk of failing therapy. Compared to uncomplicated UTIs, complicated UTIs are typically more difficult to treat due to higher rates of resistance. Almost all complicated UTIs require hospital-based therapy, accounting for most of the 3 million to 4 million UTIs treated in the hospital setting on an annual basis. There is a significant unmet need for an effective oral treatment option for drug-resistant complicated UTIs, and we believe that ETX0282CPDP has the potential to be used in the hospital setting as an oral stepdown from a short course of IV therapy or to avoid hospital admission in the first place.

ETX0282 is a potential best-in-class oral BLI, which we designed to have both high oral bioavailability and broad Class A and Class C β-lactamase inhibition. To our knowledge, no other orally bioavailable treatment has a microbiological profile with coverage against both Class A and Class C β-lactamase-producing bacteria, including ESBL-producing bacterial strains and CRE. We chose to combine ETX0282 with cefpodoxime, an orally administered β-lactam that was used for the treatment of UTIs before its clinical utility was limited by β-lactamase-mediated resistance. In *in vitro* and *in vivo* analyses, we observed that ETX0282 potently restored the efficacy of cefpodoxime to be comparable or superior to existing standard-of-care IV antibiotics. We initiated a multi-part Phase 1 clinical trial of ETX0282CPDP in Australia in the second quarter of 2018. We expect to receive data from the Phase 1 trial in mid-2019.

NBPs for the treatment of multidrug-resistant Gram-negative infections

Leveraging our targeted-design platform, we are also developing a potential new class of antibiotics that are NBPs. PBPs are proteins that play an important role in bacterial cell wall synthesis, which is essential for growth and reproduction of bacteria. PBPs are a validated target for β-lactam antibiotics. NBPs are structurally distinct from β-lactams, and therefore unaffected by all four classes of β-lactamases.

This program is in the lead-optimization stage of development. In our preclinical studies, we observed anti-bacterial activity of several of our NBP inhibitors against multiple Gram-negative pathogens. Based on the results of those studies, our initial focus is on infections caused by *Pseudomonas.* We plan to generate additional microbiology, pharmacology and toxicology data to guide the design and enable selection of an initial clinical candidate in 2019. If successful in development, we believe our NBPs would be the first novel broad-spectrum Gram-negative antibiotic class developed since the carbapenems were introduced in 1985.

Our Scientific Platform

Our targeted-design platform was initially developed by AstraZeneca to address the limitations of traditional approaches to the research and development of novel antimicrobial agents. This platform has been further refined by our team at Entasis, which has significant experience in research and development at global pharmaceutical companies. All our product candidates and our preclinical program have been developed using our targeted-design platform. AstraZeneca has not retained any rights to the targeted-design platform or to any product candidates developed with the platform.

Historically, antibiotic discovery efforts have focused on screening high volumes of natural and synthetic compounds for activity against bacterial pathogens and advancing these molecules toward clinical development, providing limited predictability of safety and efficacy profiles. Such approaches have produced few effective new antibiotics in recent years. In contrast, our platform adopts a rational approach to the discovery and development of new molecules based upon four principles. First, we select clinically validated mechanisms that are well understood and for which we understand the way pathogens develop resistance. Clinically validated mechanisms are those for which prior drugs have been developed to target precedent mechanisms of antibiotic resistance, have demonstrated sufficient clinical efficacy and safety data to be approved by a regulatory agency such as the FDA, and are well established and widely used in the clinical setting. We believe this selection process reduces the risk of failure in clinical trials because we are not adopting novel, untested modalities, while our understanding of antibacterial resistance enables us to design molecules that retain activity against pathogens that have become resistant to older antibiotics. Second, to design such molecules with activity against resistant strains, we utilize bacterial genomics and state-of-the-art molecular and dynamic models, which allow us to understand and predict the way in which our molecules attach themselves to their target, as well as the way in which they penetrate the Gram-negative envelope. Third, throughout the design process we incorporate knowledge gained from preclinical pharmacokinetic and safety studies, as well as pharmacodynamic modeling, to select molecules that we believe will be safe and well tolerated in the clinic at doses that would be efficacious against the target pathogens. Fourth, we focus our clinical development on selected pathogens with high unmet medical need, rather than broad indications that can be served by other antibiotics. We believe this enables us to optimize the potency of our product candidates and define the appropriate dosing regimen against those specific pathogens, as well as leverage the streamlined development and regulatory pathways available for first-in-class or best-in-class antibiotics.

We seek to protect our proprietary and intellectual property position for our product candidates, our core technologies, and other know-how through U.S. and foreign patent protection. To the extent that our targeted-design platform is not patentable, we rely on trade secret protection and confidentiality agreements to protect our interests. For more information, see the section titled "Business—Intellectual Property."

Our Strategy

Our goal is to be a leader in the discovery, development and commercialization of novel antibacterial agents for the treatment of multidrug-resistant Gram-negative infections. Our pathogen-directed strategy includes the following key components:

- ***Rapidly advance our lead product candidate, ETX2514SUL, through a single Phase 3 trial.*** We are in the process of initiating a single Phase 3 clinical trial of ETX2514SUL in patients with pneumonia or bloodstream infections due to *Acinetobacter* and expect to receive data in the second half of 2020. Based on the results of our preclinical studies and clinical trials, we believe that ETX2514 has the potential to restore the activity of imipenem against multiple bacterial pathogens, such as CRE and carbapenem-resistant *Pseudomonas,* and we plan to collect clinical data on these pathogens in the Phase 3 trial should *Acinetobacter* patients be coinfected.

- ***Develop zoliflodacin to be the next recommended first-line treatment for uncomplicated gonorrhea.*** We also plan to initiate a single Phase 3 clinical trial of zoliflodacin in patients with uncomplicated gonorrhea in mid-2019, and we expect to receive data in 2021. This Phase 3 clinical trial will be fully funded by GARDP. We developed zoliflodacin using our targeted-design platform to utilize the same mechanism of action as fluoroquinolones while avoiding existing fluoroquinolone resistance. In our Phase 2 clinical trial, we observed a 100% cure rate of urogenital and rectal infections in the per-protocol population with a single 3.0 g oral dose of zoliflodacin. With its expected efficacy and safety profile and convenient oral dosing, we believe zoliflodacin has the potential to become the recommended first-line treatment for uncomplicated gonorrhea.

- ***Develop ETX0282CPDP as an oral treatment for complicated UTIs, including those caused by ESBL-producing bacterial strains or CRE.*** Patients with UTIs caused by bacteria that are resistant to existing oral treatment options frequently require hospital admission for treatment with IV antibiotics, even when they are otherwise healthy and fit to be treated outside the hospital setting. There is a significant unmet need for an effective oral treatment option for drug-resistant complicated UTIs, and we believe that ETX0282CPDP has the potential to be the first oral therapeutic option for the treatment of complicated UTIs with broad coverage of Gram-negative bacteria, including ESBL-producing *Enterobacteriaceae* and CRE. We initiated a multi-part Phase 1 clinical trial of ETX0282CPDP in Australia in the second quarter of 2018. We expect to receive data from the complete Phase 1 trial in mid-2019.

- ***Expand our product portfolio by leveraging our targeted-design platform.*** All our product candidates have been developed using our targeted-design platform, which provides us with the potential to expand our pipeline. For example, we are developing a potential new class of antibiotics that are NBPs. In our preclinical studies, we observed activity of several of our NBPs against multiple Gram-negative pathogens, including *Pseudomonas*. We are currently optimizing several promising compounds from this program, and we anticipate selecting an initial clinical candidate in 2019.

- ***Leverage existing and establish additional collaborations for support of our product candidates and future programs.*** We are currently collaborating with Zai Lab as well as nonprofit organizations, government agencies and other third parties, including GARDP, the U.S. National Institute of Allergy and Infectious Diseases, or NIAID, the U.S. Department of Defense and the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program, or CARB-X, which provide financial and technical support of our research and development efforts. We will continue to evaluate and pursue additional potential collaborations with academic institutions, government agencies, nonprofit entities and

pharmaceutical and biotechnology companies to support and expand our pipeline as well as achieve our strategic objectives.

- ***Establish commercialization and marketing capabilities.*** We plan to establish a specialty sales force to commercialize our product candidates in the hospital setting in the United States. Outside the United States, we plan to work with multi-national pharmaceutical companies and other collaborators to leverage their commercialization capabilities. We also plan to seek collaborators to commercialize zoliflodacin in the community setting in the territories where we have retained rights.

Antibiotics Background

The introduction of antibiotics for the treatment of bacterial infections is recognized as one of the most transformative events in medicine. After penicillin entered the market in the early 1940s, antibiotics became one of the most commonly prescribed drugs in history.

There are two main varieties of bacteria, Gram-positive and Gram-negative, which are identified using a common laboratory staining test known as the "Gram stain." Gram-positive bacteria are surrounded by a single membrane, while Gram-negative bacteria have both an inner membrane and an outer membrane. Due to this increased complexity, it has historically been more challenging to develop products that target Gram-negative bacteria, such as *Pseudomonas*, *Acinetobacter* and *Enterobacteriaceae*, a family of related organisms that includes *Escherichia coli, Klebsiella pneumonia*, or *Klebsiella*, and *Enterobacter* species. Of the estimated 25 million annual infections in the United States, approximately 8.2 million are treated in hospital. Approximately 60% of hospital-treated infections are Gram-negative, and over 200,000 patients treated in hospital for Gram-negative infections die annually in the United States.

Antibiotics are assessed by the following criteria:

- ***Spectrum:*** Antibiotics exhibiting activity against a wide variety of pathogens are broad spectrum while antibiotics only effective against a few pathogens are narrow-spectrum. Physicians commonly use broad-spectrum agents before the pathogen has been identified and narrow-spectrum agents following pathogen diagnosis.

- ***Cidality:*** Generally, antibiotics are either bacteriostatic or bactericidal. Bacteriostatic antibiotics stop bacterial growth, allowing the immune system to clear the infection. Bactericidal antibiotics kill the bacteria directly.

- ***Potency:*** An antibiotic's potency, or microbiological activity, is its ability to kill or inhibit the growth of bacteria *in vitro*. Potency is commonly measured as minimum inhibitory concentration, or MIC, which represents the lowest concentration of antibiotic required to inhibit the growth of the bacteria. Antibiotics with lower MIC values are considered more potent. When MIC values are reported with subscript digits, e.g. $MIC_{\#\#}$, these data represent the MIC associated with inhibiting the growth of at least ##% of a panel of bacterial strains. MIC_{90} values are the most common method of reporting antibiotic potency and are associated with MIC values inhibiting the growth of at least 90% of the bacterial strains tested.

- ***Tolerability:*** Antibiotics, like most drugs, are associated with various forms of adverse events. These are frequently mild and transient, such that the patient may not even exhibit symptoms. More serious issues associated with antibiotics include toxicity in the kidney and nervous system and gastrointestinal tolerability issues, which can cause dosing limitations in patients. Less commonly observed are potential life-threatening events in the form of seizures, cardiac arrhythmias or severe allergic reactions. Although antibiotic potency is necessary for an efficacious therapy, it is not sufficient to deliver clinical benefit without a favorable tolerability profile that enables safe dosing at therapeutically relevant levels.

- ***Susceptibility:*** Considering drug potency, safety, pharmacokinetic and pharmacodynamic parameters, medical standards organizations such as the Clinical Laboratory and Standards Institute, or CLSI, and the European Committee on Antimicrobial Susceptibility Testing establish MIC "breakpoints" to designate pathogens as susceptible or resistant to a particular antibiotic. Clinicians use this information to select appropriate antibiotic therapy.

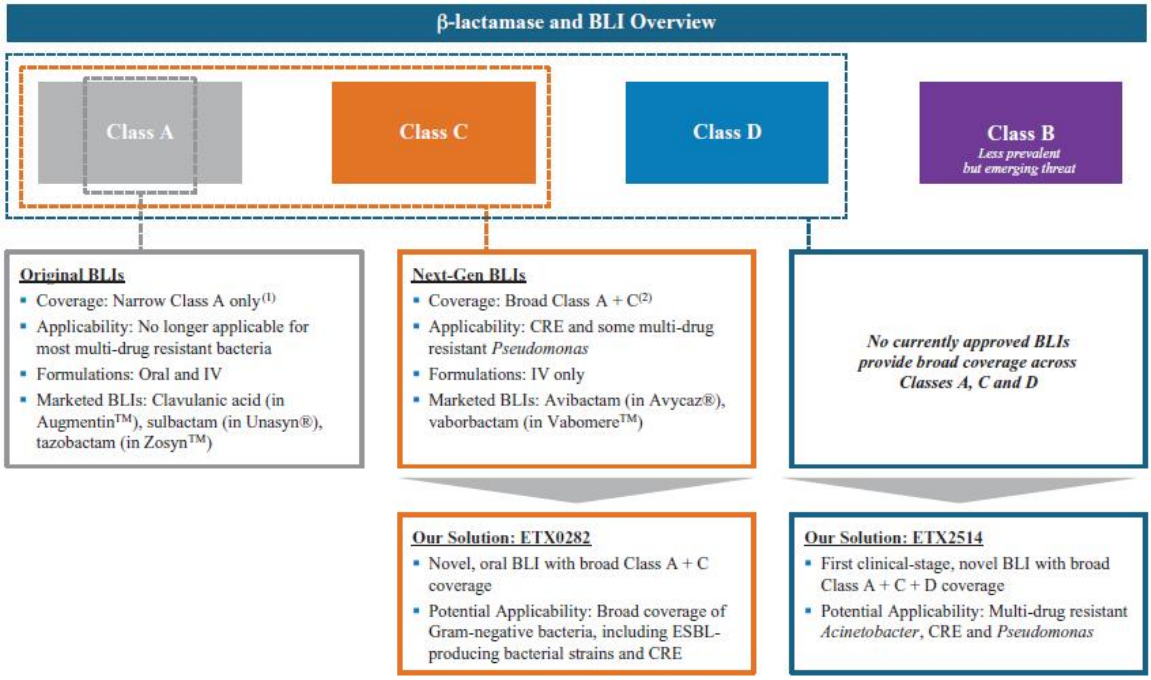
β-lactam Antibiotics

β-lactams are one of the most widely used antibiotic classes due to their attractive safety and efficacy profile. β-lactams work by inhibiting PBPs, proteins that play an important role in bacterial cell wall synthesis and are essential for the growth and reproduction of bacteria. β-lactam antibiotics were initially narrowly focused against Gram-positive bacteria but have since been developed to broadly cover both Gram-positive and Gram-negative bacteria. β-lactam antibiotics consist of all antibiotic agents that contain a β-lactam ring in their molecular structures. Among β-lactam antibiotics, penicillin derivatives and cephalosporins are the most commonly used. Carbapenems, another class of β-lactam antibiotics, are generally more effective against resistant pathogens, but to preserve their activity, they are often limited for use as a last resort.

Bacteria often develop resistance to β-lactam antibiotics by synthesizing β-lactamases, enzymes that attack the β-lactam ring. β-lactamases are widely prevalent, with over 2,800 known to date, and are classified into four classes, Classes A, B, C and D. In 1976, researchers discovered the first BLI, clavulanic acid. By inhibiting the activity of the β-lactamases, clavulanic acid could restore the potency of β-lactam agents. One of the most commercially successful antibiotics, Augmentin™, is a combination of amoxicillin, a β-lactam antibiotic, and clavulanic acid.

While additional BLIs followed clavulanic acid, bacterial pathogens continuously develop resistance by modifying or replacing the PBPs and acquiring new β-lactamases, including Class C β-lactamases and Class A carbapenemases. In response to the increasing number of β-lactamases, biopharmaceutical companies developed additional IV BLIs that inhibit a broad spectrum of Class A and Class C β-lactamases, enabling the restoration of the antibacterial activity of the β-lactam antibiotics with which they are combined. While these newer BLIs represent a significant step forward, they do not broadly inhibit Class D β-lactamases, which are a concern in infections caused by multidrug-resistant *Acinetobacter* and cannot be administered orally.

The following figure outlines the evolution of BLIs and their coverage across the β-lactamase classes.



(1) Narrow Class A β-lactamase coverage only; No coverage of ESBL and carbapenemase.
(2) Includes coverage of ESBL and carbapenemase.

Antibiotic Resistance

Antibiotic resistance is an increasingly serious threat to global public health that requires action across all government sectors and society. Antibiotic-resistant infections often result in high morbidity and, in many cases, mortality. According to the Review on Antimicrobial Resistance, over 700,000 people worldwide die each year from antibiotic-resistant infections and up to 10 million lives per year could be at risk by 2050. In the United States alone, antibiotic-resistant infections are estimated to add $20 billion per year to healthcare costs.

The evolution of bacterial resistance has outpaced the development of novel antibiotics. The Center for Disease Dynamics, Economics and Policy reported that in the United States, *E. coli* resistance to fluoroquinolones more than doubled from 2004 to 2016, surpassing 31%. *E. coli* resistance to cephalosporins quadrupled over the same period, reaching 15% in 2016. *Klebsiella* reached carbapenem and cephalosporin-resistance of 3% and 12%, respectively, in 2016. At least 10% of *Pseudomonas* infections are resistant to carbapenems, third-generation cephalosporins or fluoroquinolones in the United States. While the overall use of antibiotics in the United States and European Union dropped 1% annually from 2004 to 2015, the use of the last-resort antibiotics, carbapenems and polymyxins, increased annually 6% and 8%, respectively, over the same time period. The CDC, World Health Organization and Infectious Diseases Society of America report priority pathogens based on current treatment options and resistance rates. All three sources identify the pathogens targeted by our current product candidates, *Acinetobacter, Pseudomonas,* CRE and *N. gonorrhoeae*, as high priority.

Rising antimicrobial resistance has catalyzed a global call to action. Funding from government and nonprofit agencies for antibiotic research and development and an improved regulatory environment support the efficient development of novel antibiotics targeted at unmet need areas. NIAID, Biomedical Advanced Research and

Development Authority, Defense Advanced Research Projects Agency, the U.S. Department of Defense, GARDP and the Innovative Medicines Initiative all offer funding for the research and development of novel antibiotics.

Changes in the legal landscape in the United States have also highlighted the growing importance of addressing antimicrobial resistance. In July 2012, the Generating Antibiotic Incentives Now Act, or the GAIN Act, was adopted, which provides regulatory incentives for the development of new antibacterial or antifungal drugs intended to treat serious or life-threatening infections that are resistant to existing treatment. Legislative initiatives have recently been approved as part of the 21st Century Cures Act, including the limited-population regulatory pathways for patients with few or no suitable treatment options. Other legislation still pending includes the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms Act, which would designate certain novel antibiotics used to treat serious bacterial infections to receive higher Medicare reimbursement, and an amendment to the GAIN Act, which would allow successful qualified infectious disease product, or QIDP, sponsors to transfer up to one year of exclusivity to another product, including products marketed by other companies.

Our Product Candidates

ETX2514SUL

Overview

We are developing ETX2514SUL, a fixed-dose combination of ETX2514 with sulbactam, as a novel IV antibiotic with broad-spectrum β-lactamase coverage for the treatment of infections caused by multidrug-resistant *Acinetobacter.* Using our targeted-design platform, we engineered ETX2514 to expand the β-lactamase coverage beyond that of currently marketed BLIs. To our knowledge, unlike currently marketed BLIs, ETX2514 is the first clinical-stage BLI with broad-spectrum activity against Classes A, C and D β-lactamases.

We selected sulbactam as the β-lactam antibiotic to combine with ETX2514 based on *in vitro* and *in vivo* analyses in which we observed sulbactam's superior microbiological potency compared to other β-lactam antibiotics we studied. While sulbactam is commonly used as a BLI, it also has excellent standalone bactericidal activity against susceptible strains of *Acinetobacter,* with a long-appreciated safety and efficacy profile. Unasyn™, the fixed-dose combination of sulbactam and ampicillin, a penicillin-derived antibiotic, was frequently prescribed for the treatment of *Acinetobacter* infections until β-lactamase-mediated resistance rendered sulbactam generally ineffective. We believe that ETX2514's expanded coverage against Classes A, C and D β-lactamases gives it the potential to restore the efficacy of sulbactam against multidrug-resistant *Acinetobacter*.

Because patients with *Acinetobacter* infections may be coinfected with other bacterial pathogens, we plan to administer ETX2514SUL in combination with IMI in our clinical trials to provide broad coverage for these other pathogens. This will also provide us with clinical data on the activity of ETX2514SUL in combination with imipenem against a range of Gram-negative pathogens in addition to *Acinetobacter*. Based on the results of our preclinical studies and clinical trials, we believe that ETX2514 has the potential to restore the activity of imipenem against multiple bacterial pathogens, such as CRE and carbapenem-resistant *Pseudomonas.* We believe this may allow us to expand the clinical utility of ETX2514SUL.

Limitations of Current Treatment Options

Acinetobacter is a hospital-associated Gram-negative pathogen most commonly found in severe pneumonia, as well as bloodstream, urinary tract and wound infections. In the United States, approximately 63% of *Acinetobacter* bacteria are considered multidrug-resistant and, in 2016, select hospital antibiogram data indicate *Acinetobacter* strains tested were resistant to carbapenem antibiotics in excess of 60%. Carbapenem resistance in some European and Asian countries is reported to be even higher, surpassing 80% in some cases. Given the lack of effective treatment options, *Acinetobacter* infections can result in mortality rates approaching 50% for patients with pneumonia and bacteremia. For these reasons, the Infectious Diseases Society of America has included *Acinetobacter baumannii* among the six most threatening resistant pathogens responsible for high morbidity and mortality in patients, the CDC has classified *A.*

baumannii as a serious public health threat, and the World Health Organization included *Acinetobacter* as one of three critical pathogens on their Priority Pathogens List.

There are few treatment options available to effectively treat patients with multidrug-resistant *Acinetobacter* infections. β-lactamases are the main cause of resistance to β-lactam antibiotics, such as sulbactam, which had been widely used for the treatment of *Acinetobacter* infections prior to resistance emerging. Multiple other mechanisms of resistance, together with β-lactamases, have contributed to the emergence of *Acinetobacter* strains that are resistant to other commonly used classes of antibiotics and have made it challenging to develop new antibiotics to treat this pathogen. Consequently, multidrug-resistant *Acinetobacter* infections are now routinely treated with broad-spectrum antibiotics such as colistin, a polymyxin class antibiotic, or tigecycline, a tetracycline class antibiotic. Agents such as colistin and tigecycline show *in vitro* potency against multidrug-resistant *Acinetobacter*, but colistin can be toxic to the kidney and nervous system and tigecycline can cause gastrointestinal tolerability issues. This toxicity and intolerability can limit effective dosing, and when combined with poor tissue penetration, particularly in the lung, contribute to reduced clinical efficacy. As a result, overall mortality of patients with multidrug-resistant *Acinetobacter* infections is close to 50%, and there is an emerging threat of *Acinetobacter* strains reported to be resistant to all available antibiotic therapies, including colistin, which is currently reserved as a last-resort treatment option.

Our Solution

Data generated with ETX2514SUL suggest that our product candidate has the potential to overcome the limitations of current antibiotics for the treatment of patients with multidrug-resistant *Acinetobacter*. *Acinetobacter* resistance to β-lactams is primarily driven by the expression of Class D β-lactamases, often in combination with Class A and/or Class C β-lactamases. In our preclinical studies, we observed that ETX2514 potently inhibited Classes A, C and D β-lactamases. We believe ETX2514 is the first clinical-stage β-lactamase inhibitor with this broad spectrum of inhibition and may restore the activity of sulbactam, an antibiotic with excellent standalone bactericidal activity against susceptible strains of *Acinetobacter,* with a longstanding safety and efficacy profile. We believe ETX2514SUL may have a favorable safety profile at therapeutically active doses. Preclinical toxicology studies did not identify a dose-limiting toxicity, and ETX2514SUL was generally well tolerated in our three Phase 1 and our Phase 2 clinical trials, including at doses that are well in excess of our planned Phase 3 clinical trial dose. Based on the preclinical efficacy evaluation and preclinical and clinical tolerability profile of ETX2514SUL observed to date, we believe it has the potential to improve outcomes of patients with multidrug-resistant *Acinetobacter* infections, reducing their overall mortality and accelerating their recovery and hospital discharge, as well as to contain outbreaks of *Acinetobacter* in critical care units, leading to reduced healthcare costs.

Market Opportunity

We estimate that there are 60,000 to 100,000 hospital-treated *Acinetobacter* infections annually in the United States and as many as 120,000 annually across the major markets in Europe. Based on current carbapenem resistance rates, we estimate there are between 90,000 and 120,000 hospital-treated carbapenem-resistant *Acinetobacter* infections annually in these countries, which we regard as our initial target markets for ETX2514SUL. We also believe there could be a significant market opportunity in Asia-Pacific, given resistance rates as high as 80% in some countries. If approved, we believe ETX2514SUL has the potential to overcome the issues of resistance and tolerability limiting the effectiveness of carbapenems as well as regimens containing colistin.

Clinical Development Plan

Based on a series of discussions with the FDA, including an end-of-Phase-2 meeting, we believe that the efficacy data from the single Phase 3 clinical trial, if positive, will be sufficient to support the submission of an NDA to the FDA. We are in the process of initiating a single Phase 3 clinical trial of ETX2514SUL. The Phase 3 clinical trial will evaluate approximately 130 patients with confirmed carbapenem-resistant *Acinetobacter* hospital-acquired pneumonia, ventilator-acquired pneumonia or bloodstream infections, or a combination of these. We anticipate that this will require us to enroll approximately 220 patients with *Acinetobacter* infection, regardless of carbapenem resistance. All patients will be randomized on a 1:1 basis to receive either ETX2514SUL plus IMI or colistin plus IMI over a period of up to 14 days. The primary endpoint will be 28-day all-cause mortality, with a 19% noninferiority margin, in the

approximately 130 patients with confirmed carbapenem-resistant *Acinetobacter* infections. Noninferiority margins are used in the statistical analysis comparing two treatment arms in a trial to distinguish the degree of potential difference between the antibiotics being evaluated, with a lower margin being more difficult to achieve. Secondary endpoints will include 28-day all-cause mortality in the total enrolled patient population as well as 14 day all-cause mortality and clinical and microbiologic efficacy assessed 7 to 14 days after the end of therapy. In addition, we will evaluate the clinical and microbiologic efficacy of ETX2514SUL in combination with IMI in patients coinfected with other imipenem-resistant pathogens.

A second part of the Phase 3 clinical trial will seek to enroll approximately 80 additional patients with confirmed *Acinetobacter* infections who are not otherwise eligible for the randomized comparison, including those with infections at body sites other than the lung or bloodstream. All these patients will receive ETX2514SUL plus IMI. Data from this part of the trial will not be included in the primary endpoint efficacy analysis but may provide evidence of the effectiveness of ETX2514SUL in *Acinetobacter* infections at other body sites, such as the skin and urinary tract.

We estimate an 18-month enrollment period using 75 to 100 clinical sites for our planned Phase 3 clinical trial. To help meet our enrollment projection timeline, we have undertaken a detailed feasibility/implementation assessment to preferentially select clinical trial sites that can identify and enroll patients with high rates of carbapenem-resistant *Acinetobacter* pneumonia and bloodstream infections. Pursuant to our license and collaboration agreement with Zai Lab, Zai Lab will fund most of our clinical trial costs in China for ETX2514SUL, including all costs in China for our planned Phase 3 clinical trial of ETX2514SUL, except for patient drug supply. Zai Lab will take the lead in China by conducting the screening, enrollment and treatment of patients, and will coordinate development, registration and commercialization of ETX2514SUL in China. We are in the process of initiating the Phase 3 clinical trial and expect to receive data in the second half of 2020.

As we have done for each of our other clinical candidates, we have employed rigorous pharmacokinetic and pharmacodynamic modeling to project the efficacious ETX2514SUL dosing regimen, combining static and dynamic pharmacodynamic *in vitro* data, data from *in vivo* experiments, as well as pharmacokinetic data from preclinical studies and our Phase 1 and Phase 2 clinical trials. Our analyses suggest a 1.0 g dose of ETX2514 combined with 1.0 g sulbactam infused over three hours every six hours will deliver a therapeutically active dose in patients.

Completed Clinical Trials

We have completed three Phase 1 clinical trials including the first-in-human study, one evaluating the penetration of ETX2514SUL into the lung and one to assess pharmacokinetics in renally impaired patients. In addition, we have completed a Phase 2 clinical trial in patients with complicated UTIs. In these clinical trials, ETX2514SUL was generally well tolerated.

Our four-part Phase 1 first-in-human clinical trial was conducted in Australia in 124 healthy volunteers. ETX2514 was generally well tolerated, with no dose-related systemic adverse events or drug-related serious adverse events reported. ETX2514 also exhibited linear dose-dependent increases in exposure and pharmacokinetic parameters across the dose range studied.

Key takeaways from the four-part trial include the following:

- *Single-Ascending Dose Escalation:* ETX2514 exhibited well-behaved pharmacokinetics over the dose range of 0.25 g to 8.0 g.
- *Multiple-Ascending Dose Escalation:* ETX2514 exhibited minimal accumulation over the dose range of 0.25 g to 2.0 g infused over three hours every six hours for eight days.
- *Drug-Drug Interaction:* Co-administration of 1.0 g ETX2514 and 1.0 g sulbactam, with and without 0.5 g IMI, did not alter the pharmacokinetics of ETX2514, sulbactam, imipenem or cilastatin compared to when each was administered alone.

- *Combination Therapy Safety:* Co-administration of 1.0 g ETX2514, 1.0 g sulbactam and 0.5 g IMI, infused every six hours over a period of 11 days, was generally well tolerated with no serious adverse events or discontinuations.

There were two drug-related discontinuations in this Phase 1 clinical trial, one mild/moderate adverse event (transient drowsiness and nausea) in the 0.5 g ETX2514 multiple ascending dose escalation cohort and one moderate adverse event (transient allergic reaction symptoms) in the 1.0 g ETX2514 multiple ascending dose escalation cohort. There was also one nondrug-related serious adverse event (nut allergic reaction) during the trial, which resulted in the patient's discontinuation of the trial.

Our Phase 1 lung trial assessed the concentration of ETX2514SUL in lung fluid, an important metric to understand because the Phase 3 clinical trial will enroll patients with pneumonia and lack of appropriate lung tissue penetration has been found to contribute to reduced efficacy. ETX2514SUL was generally well tolerated, and we observed good distribution in urine and plasma as well as penetration into the lung. We believe that the levels of ETX2514SUL in the lung fluid achieved in this trial support exploring it as a potential treatment for pneumonia caused by *Acinetobacter*.

Our Phase 1 renal trial analyzed serum levels in renally impaired patients, which provided data to enable the development of a dose adjustment protocol for this type of patient, which is also the type likely to be enrolled in the Phase 3 clinical trial.

We recently completed a Phase 2 clinical trial in complicated UTI patients to provide additional safety and pharmacokinetic data as well as efficacy data against carbapenem-resistant pathogens. Eighty patients were randomized to receive either a dose of ETX2514SUL (ETX2514 1 g plus sulbactam 1 g) or placebo every six hours for seven days. Patients in both arms also received background therapy, which is current standard-of-care, with 500 mg of IMI administered through IV every six hours. ETX2514SUL was generally well tolerated. There were no serious adverse events reported and the adverse event profile of ETX2514SUL plus IMI was similar to that of the IMI comparator arm. Pharmacokinetic data observed in the Phase 2 trial was consistent with the pharmacokinetic data observed in the Phase 1 clinical trial in healthy volunteers. ETX2514SUL plus IMI showed similar microbiological success in the microbiologically evaluable population as placebo plus IMI (80% vs. 81%) and both treatment groups achieved 100% clinical success in the clinically evaluable population.

In an exploratory analysis of the Phase 2 clinical trial, we evaluated the efficacy of ETX2514SUL plus IMI against complicated UTIs caused by imipenem-non-susceptible pathogens. Eight patients had a complicated UTI caused by imipenem-non-susceptible pathogens (three in the treatment arm and five in the placebo arm). ETX2514SUL plus IMI eradicated isolates in all patients (100% [3/3]) compared to 60% (3/5) in patients receiving placebo plus IMI.

The safety data from this Phase 2 clinical trial will be used in combination with our other clinical trials to support the submission of an NDA to the FDA. We are in the process of initiating a single Phase 3 clinical trial of ETX2514SUL and expect to receive data from the trial in the second half of 2020. In addition, the efficacy data against carbapenem-resistant pathogens may inform the potential of ETX2514SUL to restore the activity of imipenem against multiple other bacterial pathogens, such as CRE and carbapenem-resistant *Pseudomonas.* We believe this may allow us to expand the clinical utility of ETX2514SUL.

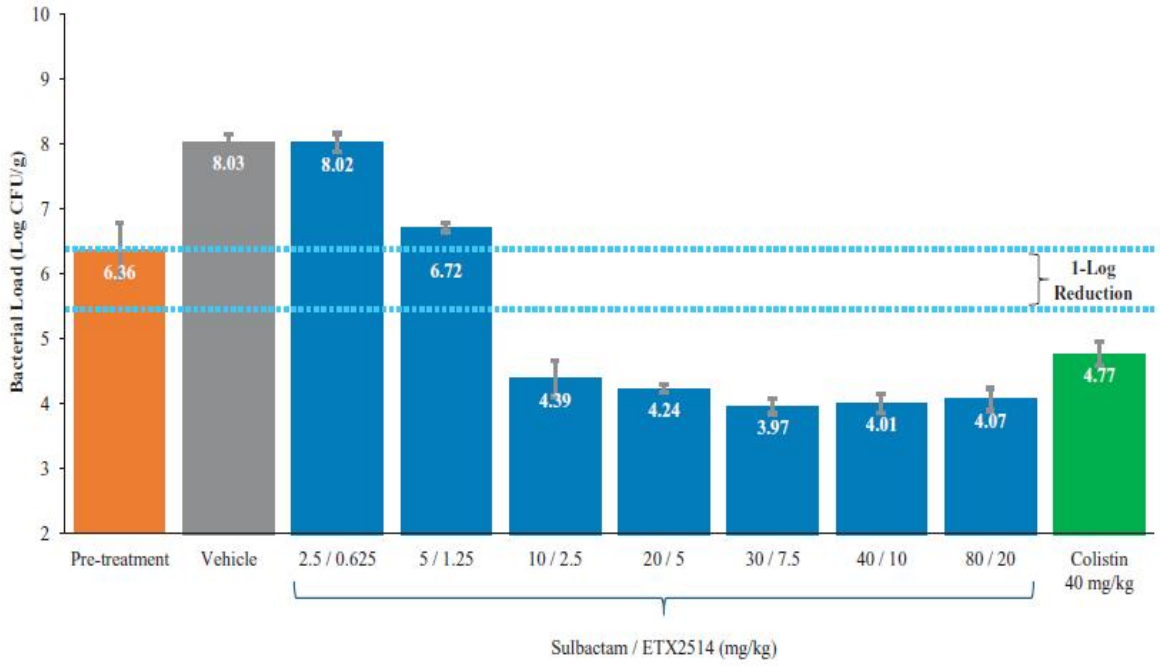
We submitted an investigational new drug application, or IND, for ETX2514SUL to the FDA in June 2017, and the FDA notified us in July 2017 that we may proceed with this program. The FDA granted Fast Track designation and qualified infectious disease product, or QIDP, designation for ETX2514SUL in September 2017 for the treatment of hospital-acquired and ventilator-acquired bacterial pneumonia and bloodstream infections due to *Acinetobacter*.

Preclinical Data

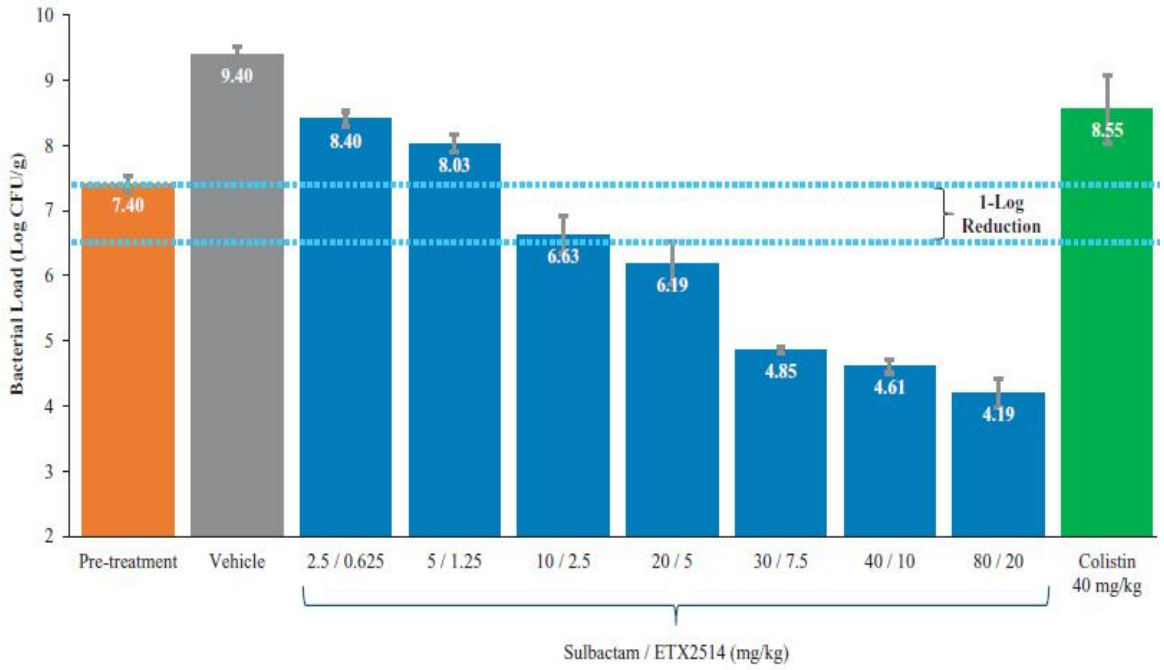
We designed ETX2514 to achieve broad activity against a wide range of β-lactamases, including Classes A, C and D, unlike currently marketed BLIs that primarily cover only Class A and Class C β-lactamases. To our knowledge, ETX2514 is the first BLI in clinical development with such a broad spectrum of *in vitro* activity. We have generated

biochemical, microbiological and *in vivo* preclinical data on ETX2514SUL. For example, mice infected with an extensively multidrug-resistant *Acinetobacter* strain in either a lung infection model or thigh infection model exhibited significant bacterial load reduction when treated with clinically relevant doses of ETX2514SUL, as shown in the figures below. Bacterial load in these figures is shown on a logarithmic scale, with each "Log" representing a 10-fold change. Accordingly, a 2-Log decrease in bacterial load represents a 100-fold decrease. A decrease of 1-Log in bacterial load is a commonly used benchmark in *in vivo* antibacterial studies to suggest that a compound may have therapeutic activity in humans. We have used this data in our pharmacokinetic and pharmacodynamic modeling to project the efficacious ETX2514SUL dosing regimen of 1.0 g ETX2514 combined with 1.0 g sulbactam infused over three hours every six hours.

***In Vivo* Activity of ETX2514 + Sulbactam in Mouse Thigh Infection Model**



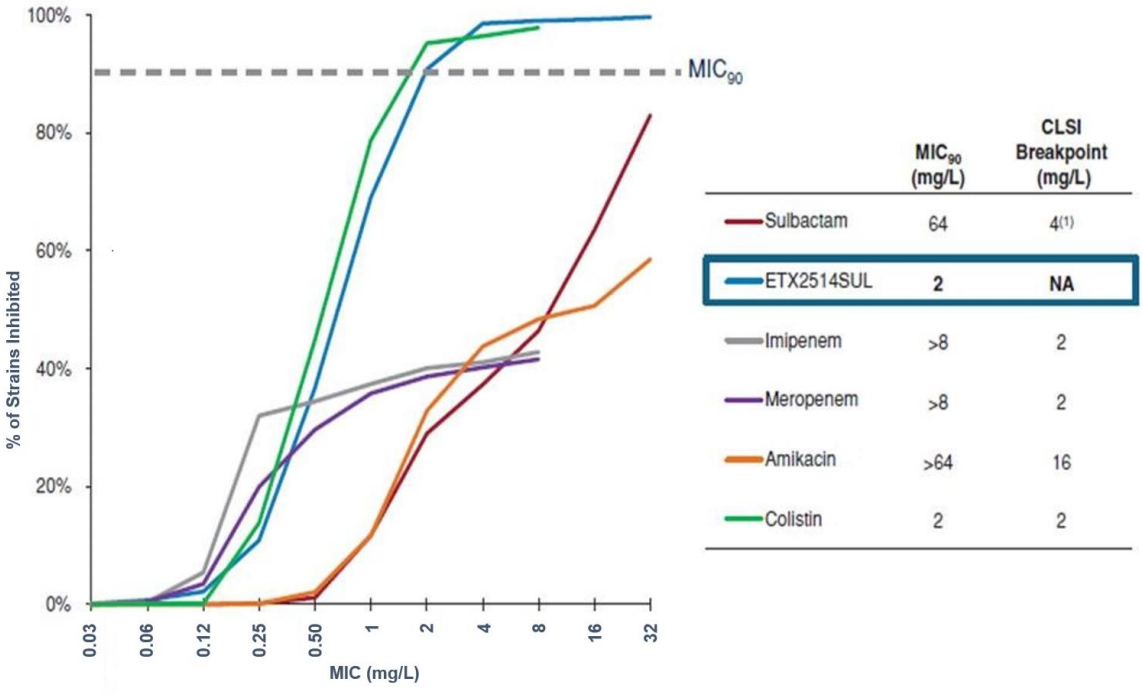
***In Vivo* Activity of ETX2514 + Sulbactam in Mouse Lung Infection Model**[1]



(1) ETX2514, sulbactam and colistin were dosed subcutaneously. Colistin was injected to the maximum tolerated dose.

ETX2514SUL has also exhibited potent microbiological activity against *Acinetobacter* strains *in vitro*. In one set of studies, we compared the effectiveness of ETX2514SUL, sulbactam alone and several marketed antibiotics in inhibiting 3,658 recent strains of *Acinetobacter*. We tested sulbactam, ETX2514SUL, imipenem and meropenem against these strains, and amikacin and colistin against 3,050 of the 3,658 strains. The plot in the figure below presents the cumulative percentage of these strains inhibited by increasing concentrations of each of the tested compounds. Sulbactam alone, as well as most of the other marketed antibiotics, had very high MIC_{90} values of 64 mg/L or higher, meaning that concentrations of 64 mg/L or greater were required to inhibit 90% of the strains. The corresponding CLSI breakpoints, which are the specified concentrations for each antibiotic that define whether a strain is considered resistant, are significantly lower than their MIC_{90} values. If the MIC_{90} of a drug is lower than its CLSI breakpoint, then that drug would be expected to be effective against more than 90% of the strains. If a drug's MIC_{90} is higher than its breakpoint, the drug would not be expected to have broad efficacy against those strains. The data in this study suggests that these recent strains of *Acinetobacter* are resistant to all the comparator antibiotics other than colistin, reflecting their significantly diminished clinical utility against *Acinetobacter* infections. In contrast, ETX2514SUL had very potent activity, with a much lower MIC_{90} of 2 mg/L. This is lower than the CLSI breakpoint for sulbactam, which is 4 mg/L (in Unasyn), suggesting that our chosen target exposure levels of ETX2514SUL may be effective against more than 90% of *Acinetobacter* strains.

***In Vitro* Activity of ETX2514SUL Against 3,658 *Acinetobacter* Strains**



(1) Based on the breakpoint for Unasyn™, the fixed-dose combination of sulbactam and ampicillin.

In this study, the 2 mg/L MIC_{90} of ETX2514SUL was equivalent to colistin, which also had a 2 mg/L MIC_{90} against 3,050 of these *Acinetobacter* strains. However, despite its microbiological activity, colistin can be toxic to the kidney and nervous system. This toxicity can limit effective dosing, and when combined with poor tissue penetration, especially in the lung, contribute to reduced clinical efficacy, consistent with the lack of efficacy observed in the mouse lung infection model above.

In addition, we have evaluated ETX2514 in 14-day toxicology studies complying with FDA good laboratory practices, or GLP, in rats and dogs, which showed no dose-limiting toxicities at doses up to 2,000 mg/kg, the upper limit dose set by the FDA.

Potential for ETX2514 to address additional Gram-negative pathogens

Classes A, C and D β-lactamases have spread not only to *Acinetobacter* but also to other Gram-negative pathogens, such as *E. coli*, *Klebsiella* and *Pseudomonas*, allowing these pathogens to develop resistance to carbapenems and cephalosporins. To target these other key pathogens, we measured their susceptibility to ETX2514 combined with imipenem. In our preclinical studies, ETX2514 improved the overall potency of imipenem across hundreds of strains of *E. coli*, *Klebsiella* and *Pseudomonas*. The figure below shows the MIC_{90} values of imipenem alone and in combination with ETX2514 for these three key pathogens. Based on this preclinical data, we believe that ETX2514SUL in combination with IMI has the potential to be a novel and potent broad-spectrum agent for treating infections caused by

E. coli, *Klebsiella* and *Pseudomonas*. To further evaluate our preclinical observations, microbiological data against these pathogens will be collected throughout our Phase 2 and Phase 3 clinical trials.

	MIC_{90} (mg/L)		
	E. coli *202 strains*	***Klebsiella*** *198 strains*	***Pseudomonas*** *1,202 strains*
Imipenem	0.25	1	16
ETX2514 + Imipenem	≤0.06	0.12	2

Zoliflodacin

Overview

We are collaborating with GARDP to co-develop zoliflodacin in a Phase 3 clinical trial for the treatment of uncomplicated gonorrhea. Uncomplicated gonorrhea is *N. gonorrhoeae* infections of the urethra, cervix, pharynx or rectum, and are more common than complicated gonorrhea. GARDP will fund all the Phase 3 development costs and will receive commercial rights for zoliflodacin in low-income and specified middle-income countries. We have retained commercial rights in all other countries, including the major markets in North America, Europe and Asia-Pacific.

Using our targeted-design platform, we are developing zoliflodacin, which is designed to utilize the same mechanism of action as fluoroquinolones while avoiding existing fluoroquinolone resistance. Fluoroquinolones bind to and inhibit bacterial gyrase, an essential bacterial enzyme, effectively disrupting the process of DNA synthesis in the bacteria and its ability to reproduce. Their widespread use against gonorrhea as well as other bacterial infections has led to gyrase mutations, resulting in the emergence of fluoroquinolone resistance. We developed zoliflodacin to target bacterial gyrase in a different manner, avoiding existing fluoroquinolone resistance while retaining potent activity against drug-resistant *N. gonorrhoeae* strains, including ESC-resistant strains. Zoliflodacin is, to our knowledge, the only novel treatment in development that provides a potential oral alternative to intramuscular injections of ceftriaxone for the treatment of drug-resistant gonorrhea.

Limitations of Current Treatment Options

N. gonorrhoeae is the bacterial pathogen responsible for gonorrhea, an extremely prevalent sexually transmitted disease that affects an estimated 78 million people worldwide each year. Gonorrhea can be associated with serious complications, including pelvic inflammatory disease, ectopic pregnancy and infertility, as well as an increased risk of HIV. Fluoroquinolone antibiotics, notably ciprofloxacin and cephalosporin antibiotics, notably cefixime, had been widely used for the treatment of gonorrhea due to their oral administration along with a favorable efficacy and safety profile. However, widespread use of these antibiotics drove the emergence of resistant *N. gonorrhoeae* strains, and as a result, treatment guidelines were amended. Ceftriaxone, an ESC, is currently the only recommended treatment option for the treatment of gonorrhea and is commonly administered with azithromycin, a broad-spectrum antibiotic, to provide coverage against other sexually transmitted diseases that tend to occur concurrently with gonorrhea. Ceftriaxone is administered by intramuscular injection, which can be painful and may require patient monitoring by a healthcare administrator. Ceftriaxone remains effective in most of the United States; however, in Hawaii as well as in several countries, including China, Japan, France and Spain, *N. gonorrhoeae* strains with decreased susceptibility to ceftriaxone have been reported, prompting concerns that multidrug-resistant gonorrhea may become a major community health issue.

Our Solution

We believe zoliflodacin has the potential to address emerging resistance issues and treat drug-resistant gonorrhea. Our oral product candidate targets the well-validated mechanism of action of the fluoroquinolone class of antibiotics but does so in a novel manner that avoids existing resistance. In our Phase 2 clinical trial, we observed a 100% cure rate of urogenital and rectal infections in the per-protocol population with a single 3.0 g oral dose of zoliflodacin. We believe a convenient single oral dosing option would be the preferred treatment option by patients, and has the potential to facilitate expedited partner therapy, which is the clinical practice of treating sexual partners of patients diagnosed with gonorrhea by providing prescriptions or medications to the patient to take to his or her partner without the healthcare provider first examining the partner. We believe zoliflodacin has the potential to reduce the spread of this highly communicable disease and, in doing so, reduce overall health care costs, including costs associated with serious complications associated with gonorrhea.

Market Opportunity

In 2012, the incidence of gonorrhea in the United States and major European countries exceeded 2.2 million cases. The CDC estimates that over 820,000 new gonorrhea infections occur annually in the United States. In a study based on data from the World Health Organization, it was estimated that in 2012 there were approximately 1.4 million gonorrhea infections in Europe and nearly 11.4 million gonorrhea infections in the Western Pacific region, which includes China and Australia. Historically, to reduce the risk of spreading drug-resistant pathogens in gonorrhea, the CDC has changed treatment guidelines when resistance rates to recommended first-line treatments reach 5%. As resistance to ceftriaxone increases, we believe zoliflodacin, if approved, could be the next product recommended for the treatment of uncomplicated gonorrhea.

Clinical Development Plan

In July 2017, we announced a collaboration with GARDP to co-develop zoliflodacin in a multi-national Phase 3 clinical trial, which we anticipate initiating in mid-2019 with data expected in 2021. GARDP will conduct the Phase 3 clinical trial and will fund all the Phase 3 development costs. GARDP will receive commercial rights for zoliflodacin in low-income and specified middle-income countries. We have retained commercial rights in all other countries, including the major markets in North America, Europe and Asia-Pacific.

Based on our discussions with the FDA at our end-of-Phase-2 meeting, the Phase 3 clinical trial will be a multi-center, open-label, noninferiority trial in approximately 600 evaluable patients with uncomplicated gonorrhea who will be randomized on a 2:1 basis to receive either a single oral dose of zoliflodacin or a regimen of intramuscular ceftriaxone plus oral azithromycin. The primary endpoint will be the proportion of patients with microbiological cure at urethral or cervical sites, approximately six days after treatment. The noninferiority margin for the primary efficacy endpoint in this trial will be 10%. Secondary endpoints include the proportion of patients with microbiological cure at rectal or pharyngeal sites and the proportion of all patients with clinical cure, each measured when tested on a date that will be between four and eight days after receiving treatment. Based on our discussions with the FDA, we believe that the efficacy data from this single Phase 3 clinical trial, if positive, along with the data from our other clinical trials of zoliflodacin, will be sufficient to support the submission of an NDA to the FDA.

Phase 2 Clinical Proof-of-Concept and Phase 1 Clinical Trials

We have completed a multi-center, randomized, open-labeled Phase 2 clinical trial comparing a single oral dose of 2.0 g or 3.0 g of zoliflodacin to 500 mg intramuscular ceftriaxone for the treatment of uncomplicated gonorrhea. In this trial, zoliflodacin was generally well tolerated, with efficacy outcomes comparable to ceftriaxone. In this clinical trial, 179 randomized patients received treatment. Microbiological eradication and clinical cure in urogenital infections with a single dose of zoliflodacin, the primary endpoint of the trial, was comparable to ceftriaxone, with 100% cure in both the 3.0 g zoliflodacin and ceftriaxone groups in the per-protocol population. We also studied several exploratory endpoints, including cure rates in rectal and pharyngeal infections. In the per-protocol population, in rectal infections, six out of six patients were cured in the 3.0 g zoliflodacin group compared with three out of three patients cured in the

ceftriaxone group, and in pharyngeal infections, seven out of nine patients were cured in the 3.0 g zoliflodacin group compared with four out of four patients cured in the ceftriaxone group.

Prior to advancing to the Phase 2 clinical trial, we evaluated zoliflodacin in two Phase 1 clinical trials studying 72 healthy volunteers in total. In one trial, we evaluated pharmacokinetics and tolerability in 48 subjects and food effects in 18 subjects, and in the second trial, we evaluated absorption, distribution, metabolism and excretion in six subjects. Zoliflodacin as a single dose was generally well tolerated in these trials at doses, we would expect to be clinically active for treating uncomplicated gonorrhea. Administration of a high-fat meal was associated with an increase in zoliflodacin plasma concentration, suggesting that zoliflodacin could be administered with or without food.

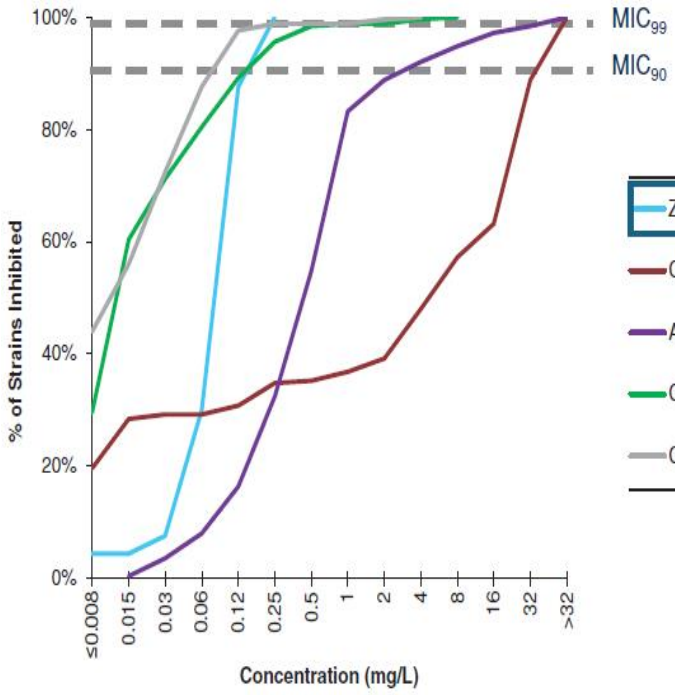
Our zoliflodacin granule formulation was evaluated in eight subjects to assess its relative bioavailability and tolerability to the prior formulation. This study demonstrated pharmacokinetic and tolerability comparable to the dosage form used in the Phase 1 single-ascending dose trial. The trial was sponsored and conducted by NIAID. This study was followed by a formal Thorough QT, or TQT study, which is a typical requirement for approval of a new chemical entity by the FDA. The purpose of a TQT study is to determine whether a drug influences cardiac rhythm. Patient enrollment is complete in the TQT study and we anticipate a full data set in the second quarter of 2019. The TQT study was also sponsored and conducted NIAID. The remaining Phase 1 trial is evaluating the administration of a high-fat meal on zoliflodacin plasma concentrations and tolerability in healthy volunteers. Enrollment is complete in the study and we anticipate a full data set in the second quarter of 2019. The clinical trial was sponsored and conducted by GARDP.

The completed Phase 1 clinical trials were conducted pursuant to an IND submitted to the FDA in August 2013 by AstraZeneca. The completed Phase 2 clinical trial was conducted under a NIAID-sponsored IND which cross referenced the original AstraZeneca IND submitted in 2013. The AstraZeneca IND was transferred to Entasis in 2015. The planned Phase 3 clinical trial is expected to be conducted pursuant to an IND submitted by GARDP.

Preclinical Data

We have generated biochemical, microbiological and *in vivo* data on zoliflodacin. In the figure below, we show a summary of *in vitro* MIC data for zoliflodacin and currently marketed antibiotics against 250 recent strains of *N. gonorrhoeae* from North America, Europe and Asia-Pacific that were selected based on their resistance phenotype. The plot in the figure below presents the cumulative percentage of these 250 strains inhibited by increasing concentrations of each of the tested compounds. The data suggest that zoliflodacin retains activity against bacterial strains that are resistant to other antibiotic classes, which was expected given its novel mechanism of action. In addition, the data show significant resistance against two of the four standard antibiotics indicated for gonorrhea, ciprofloxacin, a fluoroquinolone, and azithromycin, a macrolide, as the MIC_{90} values are much higher than the susceptibility breakpoints for each.

***In Vitro* Activity of Oral Zoliflodacin Against 250 *N. Gonorrhoeae* Strains**



	MIC90 (mg/L)	MIC99 (mg/L)	CLSI Breakpoint (mg/L)
Zoliflodacin (Oral)	0.25	0.25	NA
Ciprofloxacin (Oral)	>32	>32	0.06
Azithromycin (Oral)	4	>32	0.25(1)
Cefixime (Oral)	0.25	4	0.25
Ceftriaxone (Intramuscular)	0.12	2	0.25

(1) Breakpoint established by European Committee on Antimicrobial Susceptibility Testing.

ETX0282CPDP

Overview

We are developing ETX0282CPDP, an oral fixed-dose combination of ETX0282 with cefpodoxime, a generic cephalosporin, for the treatment of complicated UTIs, including those caused by ESBL-producing bacterial strains or CRE. Using our targeted-design platform, we engineered ETX0282 to inhibit Class A and Class C β-lactamases, which are the primary mechanisms of resistance associated with multidrug-resistant *Enterobacteriaceae* infections. We selected cefpodoxime as the β-lactam antibiotic to combine with ETX0282 following *in vitro* studies in which cefpodoxime exhibited superior activity against multidrug-resistant *Enterobacteriaceae* compared to other existing oral β-lactams. Cefpodoxime was once used to treat UTIs, among other indications, but its clinical utility is currently limited by β-lactamase-mediated resistance. We believe ETX0282 has the potential to restore the efficacy of cefpodoxime against multidrug-resistant *Enterobacteriaceae.*

While other combinations of β-lactam/BLI covering Class A and Class C β-lactamases have recently been approved for the treatment of complicated UTIs, they are only administered intravenously. We believe the oral formulation of ETX0282CPDP has the potential to be used in the hospital setting as an oral stepdown from a short course of IV therapy or to avoid hospital admission in the first place. We initiated a multi-part Phase 1 clinical trial of ETX0282CPDP in Australia in the second quarter of 2018.

Limitations of Current Treatment Options

UTIs are one of the most common bacterial infections in the United States, with up to 15 million cases occurring annually, of which we estimate that 4.0 million are complicated. *Enterobacteriaceae* species cause approximately 85% of UTIs. *E. coli* is the primary UTI pathogen, causing approximately 75% of infections. Most UTIs are treated with existing oral therapies in the community setting. However, the emergence of multidrug-resistant bacteria, including ESBL-producing bacterial strains and CRE, has reduced the efficacy of commonly used oral antibiotics such as levofloxacin and ciprofloxacin, both fluoroquinolones, and trimethoprim/sulfamethoxazole. In the United States, approximately 31% of UTIs caused by *E. coli* and 10% of UTIs caused by *Klebsiella* are resistant to fluoroquinolones. Patients with UTIs caused by bacteria resistant to existing oral treatment options frequently require hospital admission for treatment with IV antibiotics, even when they are otherwise healthy and fit to be treated outside the hospital setting. Hospital admission not only leads to inconvenience for the patient and to high treatment cost for the healthcare system, but it also increases the risk of transmitting drug-resistant bacterial strains to other hospitalized patients and exposing UTI patients to more serious hospital-acquired infections.

The unmet medical need for an oral treatment of drug-resistant UTIs has led to significant efforts to discover and develop new agents. However, to our knowledge, most of these efforts consist of redevelopment or reformulation of older oral antibiotics that lack activity against a broad spectrum of ESBL-producing bacterial strains and CRE.

Our Solution

We believe ETX0282CPDP has the potential to be the first oral therapeutic option for the treatment of complicated UTIs with broad coverage of Gram-negative bacteria, including ESBL-producing *Enterobacteriaceae* and CRE. Cefpodoxime is a well-known β-lactam antibiotic approved in 1992 for UTIs and other indications, and clinicians have an extensive history of using this antibiotic successfully until resistance emerged due to Class A and Class C β-lactamases. ETX0282 is an orally bioavailable BLI, which has the potential to protect cefpodoxime from degradation, effectively restoring its activity against drug-resistant pathogens, including ESBL-producing *Enterobacteriaceae* and CRE. If approved, we believe ETX0282CPDP will provide clinicians a convenient, oral option to treat patients suffering from complicated UTIs caused by these multidrug-resistant pathogens, which could enable early hospital discharge following a short course of IV antibiotics or the avoidance of hospital admission in the first place.

Market Opportunity

The only approved oral β-lactam/BLI combination is amoxicillin/clavulanate, which has been marketed as Augmentin™ since 1981 for treatment of UTIs and several other infections. Augmentin is one of the most commercially successful antibiotics ever launched, achieving peak worldwide sales above $2.0 billion in 2001. Augmentin demonstrated the utility of an oral β-lactam/BLI combination, but it is not effective against ESBL- and carbapenemase-producing bacterial strains, which are growing in prevalence.

We are initially developing ETX0282CPDP for the treatment of complicated UTIs which are typically more difficult to treat than uncomplicated UTIs due to higher rates of resistance. We believe that approximately 15 million UTIs occur annually in the United States, of which we estimate that 4.0 million are complicated. Almost all complicated UTIs require hospital-based therapy, accounting for most of the 3 million to 4 million UTIs treated in the hospital setting on an annual basis. We view these hospital-treated UTI patients as our initial target market for ETX0282CPDP, with potential expansion into the broader community setting as bacterial resistance grows. We believe ETX0282CPDP also has the potential for use beyond UTIs in other indications where multidrug-resistant *Enterobacteriaceae* are commonly found.

Clinical Development Plan

We initiated a multi-part Phase 1 clinical trial of ETX0282CPDP in Australia in the second quarter of 2018. The Phase 1 clinical trial is randomized, double-blind and placebo-controlled and will be conducted in five parts. The trial design is similar to that of the completed Phase 1 clinical trial of ETX2514, comprising single-ascending dose escalation, multiple-ascending dose escalation, drug-drug interaction between ETX0282 and cefpodoxime, and combination therapy

safety cohorts, but will also include a cohort to evaluate the effect of food on ETX0282CPDP's oral bioavailability. In the single-ascending dose portion of the trial, 4 out of 36 subjects experienced mild to moderate emesis (vomiting). We are in the process of analyzing data from these healthy volunteers as well as exploring options to mitigate this effect, including co-administration with food and modified release formulations. If successful, data from the Phase 1 trial will support dose selection for our subsequent clinical trials. We expect to receive data from the Phase 1 trial in mid-2019. We held a pre-IND meeting with the FDA in March 2018 and are incorporating the FDA's feedback into our clinical development plan for ETX0282CPDP.

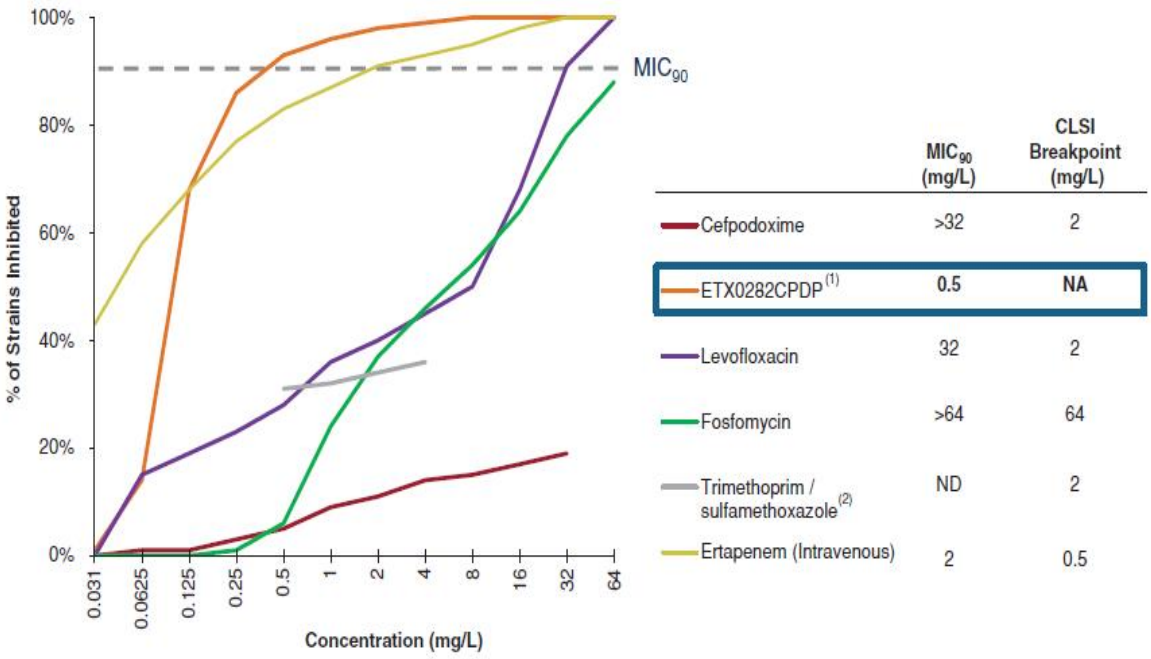
Preclinical Data

Using biochemical analysis, structure-assisted drug design and medicinal chemistry, we engineered ETX1317, a potent, broad-spectrum Class A and Class C BLI, and ETX0282, its orally bioavailable prodrug. When the prodrug, ETX0282, is taken orally, its active molecule, ETX1317, is released in the body. Similarly, cefpodoxime proxetil is the prodrug of cefpodoxime, the active form of the drug, as shown in the following table:

	Prodrug	Active Agent
β-lactam	Cefpodoxime proxetil (CPDP)	Cefpodoxime (CPD)
β-lactamase inhibitor	ETX0282	ETX1317

We have generated microbiological and *in vivo* preclinical data on ETX0282CPDP as well as on ETX1317 in combination with CPD. In one set of studies, we compared the activity of ETX1317 in combination with CPD, CPD alone and four marketed oral antibiotics in inhibiting 910 strains of *Enterobacteriaceae*, including ESBL- and carbapenemase-producing bacterial strains, collected from patients with complicated UTIs between 2013 and 2015 from a variety of countries around the world, including the United States and in Europe. We believe this collection of bacterial strains is representative of the type of pathogens found in complicated UTI patients who are likely to have failed standard-of-care oral antibiotic therapy. Approximately 90% of these bacterial strains were cefpodoxime-resistant and approximately 55% of these cefpodoxime-resistant strains were also resistant to both levofloxacin and trimethoprim/sulfamethoxazole. Approximately 70% of the bacterial strains produced ESBLs and 7% were carbapenem-resistant. We compared ETX1317 in combination with CPD to levofloxacin, an approved oral fluoroquinolone, to fosfomycin and trimethoprim/sulfamethoxazole, other commonly used oral antibiotics, and to ertapenem, a carbapenem antibiotic that is administered either intramuscularly or intravenously. The plot in the figure below presents the cumulative percentage of these 910 strains inhibited by increasing concentrations of each of the tested compounds. CPD alone and the other marketed antibiotics have MIC_{90} values that are higher than their CLSI breakpoints, indicating limited usefulness as treatment options for multidrug-resistant complicated UTIs. In contrast, ETX1317 in combination with CPD had very potent activity, with a much lower MIC_{90} of 0.5 mg/L. This study suggests that ETX0282CPDP has microbiological potency superior to the other oral antibiotics evaluated and has the potential to provide an oral alternative to IV antibiotics for patients who have failed these other therapies.

***In Vitro* Activity of ETX0282CPDP[(1)] Against 910 *Enterobacteriaceae* Strains, Including ESBL-Producing Bacterial Strains and CRE**

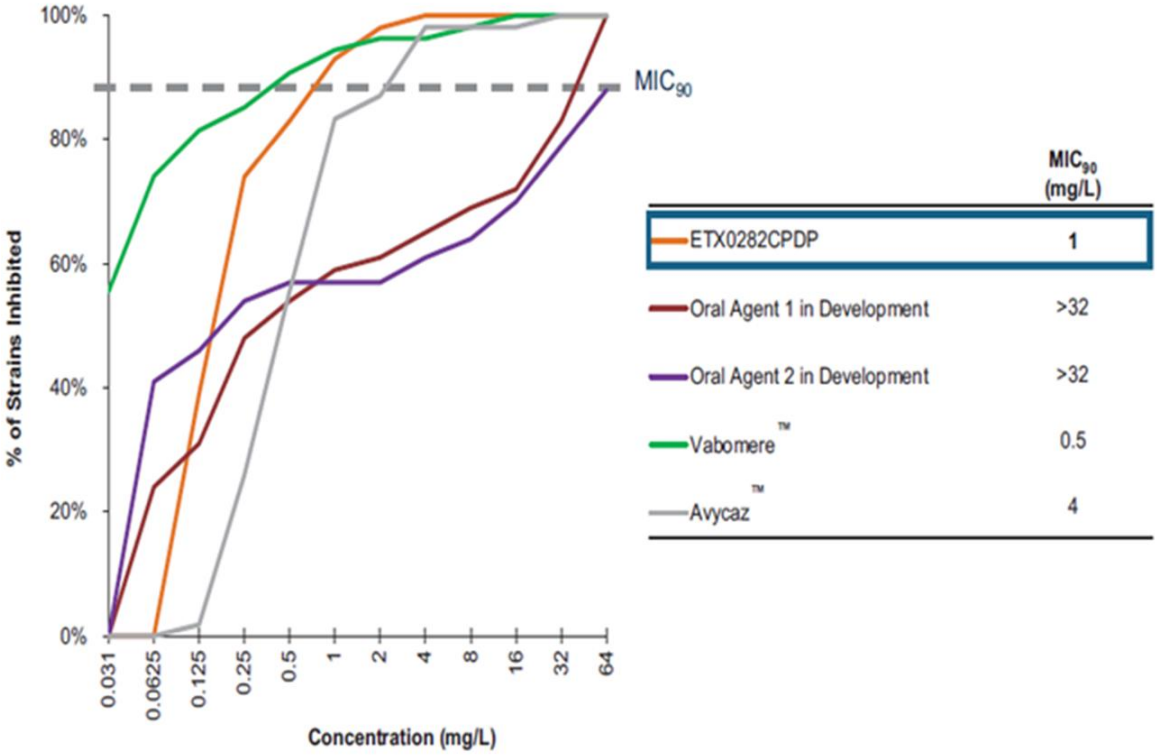


(1) ETX0282CPDP is an oral prodrug which is metabolized into ETX1317, the active BLI, and cefpodoxime. The *in vitro* activity is of ETX1317 + cefpodoxime.

(2) MIC_{90} was not determined for trimethoprim / sulfamethoxazole at the concentrations tested (0.5 mg/L to 4 mg/L).

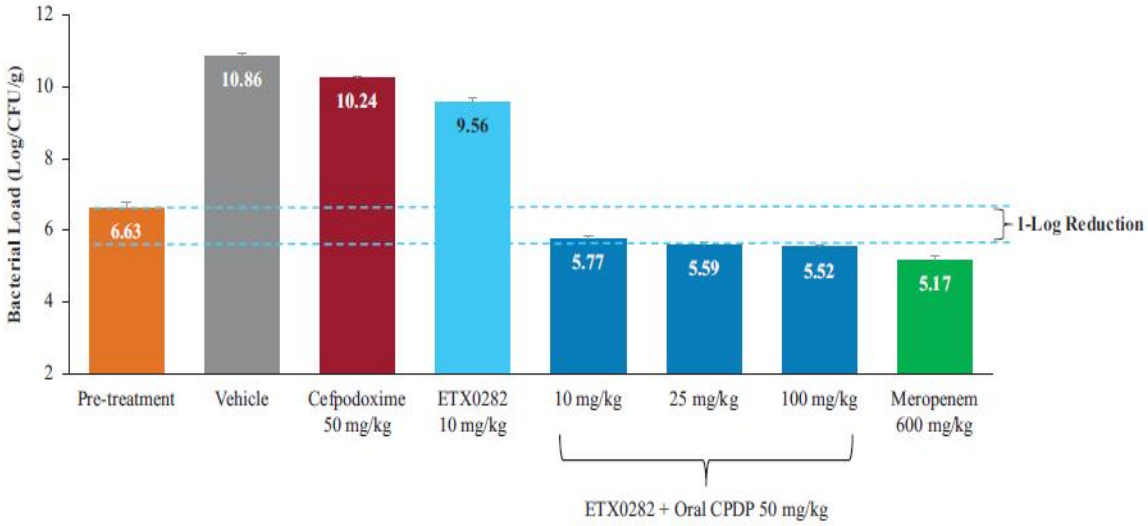
In another study, we compared the activity of ETX1317 in combination with CPD and four other antibiotics, two of which are oral agents in clinical development and two of which are marketed IV antibiotics, Vabomere™ and Avycaz™, in inhibiting 54 strains of multidrug-resistant *Enterobacteriaceae*, including CRE, collected from complicated UTI patients between 2007 and 2016. Approximately 37% of these bacterial strains were CRE. We believe this collection of strains is representative of the type of pathogens found in complicated UTI patients who are likely to have failed initial IV antibiotic therapy. The plot in the figure below presents the cumulative percentage of these 54 CRE clinical isolates inhibited by increasing concentrations of each of the tested compounds. Both oral in-development antibiotics had MIC_{90} values of 32 mg/L or higher. In contrast, ETX1317 in combination with CPD had a MIC_{90} value of 1 mg/L, similar to those of the two marketed IV antibiotics.

***In Vitro* Activity of ETX0282CPDP Against 54 *Enterobacteriaceae* Strains, Including CRE**



An important step in developing agents for oral administration is to measure oral bioavailability in preclinical studies. In our preclinical studies, the oral prodrug ETX0282 had high oral bioavailability across three species, rats, dogs and monkeys, with bioavailability of 98%, 97% and 78%, respectively. The oral bioavailability of cefpodoxime, which we are combining with ETX0282, is well established through extensive clinical use. Importantly, the active molecule, ETX1317, has pharmacokinetic properties in both rats and dogs that are compatible with the pharmacokinetic properties of cefpodoxime, which is important as ETX1317 acts by protecting cefpodoxime against degradation by β-lactamases. In a thigh infection model of mice infected with an *E. coli* strain known to be resistant to fluoroquinolones and cephalosporins, orally administered ETX0282CPDP exhibited *in vivo* bactericidal activity comparable to that of the study control, meropenem, a carbapenem antibiotic that is administered intravenously.

***In Vivo* Activity of Oral ETX0282 in Mouse Thigh Model**



Based on the data from multiple similar *in vivo* experiments, we believe that ETX0282CPDP can achieve clinically efficacious exposures with a 500 mg dose of ETX0282 and a 400 mg dose of cefpodoxime, administered orally twice daily.

In addition, we have evaluated ETX0282 in a range of *in vitro* and *in vivo* preclinical safety studies, including two 14 day GLP toxicology studies conducted in rats and dogs. These studies were supportive of progression of ETX0282 to the clinic.

NBP Program

Overview

Leveraging our targeted-design platform, we are developing a potential new class of antibiotics that are NBPs. NBPs are structurally distinct from β-lactams and therefore unaffected by all four classes of β lactamases. In our preclinical studies, we observed activity of several of our NBP molecules against multiple Gram-negative pathogens. Based on the results of those studies, our initial focus is on infections caused by *Pseudomonas* and we plan to generate additional microbiology, pharmacology and toxicology data to enable design and selection of an initial clinical candidate in 2019. Subsequently, we intend to evaluate further candidates directed against additional serious Gram-negative pathogens. If successful in development, we believe our NBPs would be the first novel, broad-spectrum Gram-negative antibiotic class since the carbapenems were introduced in 1985.

Limitations of Current Treatment Options

Infections caused by multidrug-resistant *Pseudomonas* are some of the most difficult to treat bacterial infections today. Carbapenems and cephalosporins are commonly used to treat susceptible cases of *Pseudomonas.* However, in the United States, approximately 20% of *Pseudomonas* strains are resistant to both classes of antibiotics. Some recently approved antibiotics demonstrate improved efficacy against *Pseudomonas* but are still prone to multiple mechanisms of resistance. In many cases, the only treatment option for multidrug-resistant *Pseudomonas* is colistin or other antibiotics of the same class. While these antibiotics are potent in preclinical models, in practice, clinicians tend to reserve their use

as last resort treatment options due to their toxicity in the kidney and nervous system, which limits dosing and therefore, clinical efficacy.

Our Solution

Our NBPs are a novel class of PBP inhibitors that are chemically distinct from β-lactam antibiotics. While their mode of action is through PBPs, the well validated target of β-lactams, our NBPs are designed to retain activity against pathogens with pre-existing resistance from β-lactamases. If successfully developed, our NBPs could potentially be used as a monotherapy to effectively treat infections caused by multidrug-resistant *Pseudomonas* and other Gram-negative pathogens. While we believe our novel NBP class may have broad antibacterial activity against several Gram-negative pathogens, we expect the initial clinical candidate that we select from this program will aim to address the serious medical need of multidrug-resistant *Pseudomonas* infections.

Market Opportunity

Pseudomonas causes a variety of infections, including intra-abdominal infections, surgical site infections, UTIs and nosocomial pneumonia. *Pseudomonas* is the most common Gram-negative pathogen associated with ventilator-acquired pneumonia and tends to have higher resistance rates than other Gram-negative pathogens commonly causing ventilator-acquired pneumonia. *Pseudomonas* infections are on the rise with an estimated 600,000 to 750,000 cases occurring annually in the United States. In 2014, approximately 20% of *Pseudomonas* infections were resistant to each of carbapenems, cephalosporins and fluoroquinolones and 14% were resistant to at least three classes of antibiotics. We believe our novel class of NBPs has the potential to be used as monotherapy against infections caused by multidrug-resistant *Pseudomonas*.

Preclinical Data

Our NBP program is in the lead-optimization stage of development in which we are designing molecules for optimal activity against the PBP enzymes, potency against bacterial strains, as well as other desirable properties such as safety and pharmacokinetics, with the goal of selecting an initial clinical candidate for development. Our targeted-design platform has enabled us to develop several lead molecules with activity against the PBPs *in vitro*, as well as good Gram-negative pathogen permeability. In preclinical studies, including animal models of *Pseudomonas* infections, we have observed that some of our NBPs are unaffected by β-lactamases from all four Ambler classes and have shown activity against multidrug-resistant Gram-negative bacteria, in particular, *Pseudomonas.*

Commercial Strategy

We intend to directly commercialize our product candidates in the hospital setting in the United States through a targeted specialty sales force. Our commercial strategy will be to target hospitals with the greatest incidence of serious and life-threatening multidrug-resistant bacterial infections. We intend to establish ETX2514SUL, if approved, as the standard of care for carbapenem-resistant *Acinetobacter* infections and ETX0282CPDP, if approved, as the primary oral option for multidrug-resistant complicated UTIs. We designed our clinical development strategies to differentiate these product candidates from both approved and current development stage antibacterial products.

Outside the United States, we plan to work with multi-national pharmaceutical companies to leverage their commercialization capabilities. We also plan to seek collaborators to commercialize zoliflodacin in the community setting in the territories where we have retained commercial rights, including the major markets in North America, Europe and Asia-Pacific.

Supply and Manufacturing

We do not own or operate manufacturing facilities for the production of any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on a limited number of third-party contract manufacturers for all our required raw materials, drug substance, and finished drug product for our preclinical research and clinical trials. We do not have long-term agreements with these third parties. We

also do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates after they are approved. If any of our products are approved by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers for the commercial production of those products. We currently employ internal resources to manage our manufacturing.

Government and Nonprofit Awards

Through December 31, 2018, we have received aggregate financial commitments of up to $17.5 million from the Trustees of Boston University through the CARB-X program and the U.S. Army Medical Research Acquisition Activity, a division of the U.S. Department of Defense, in support of our ETX0282, NBP and discovery research programs. The CARB-X awards commit funding of $10.1 million, with the possibility of up to a total of $16.4 million in funding based on the successful completion of prespecified milestones. These specified milestones include the completion of important steps for a development-stage project such as preclinical studies or clinical trials, manufacture and formulation work, submission of regulatory applications and regulatory meetings with the FDA or comparable foreign regulator. We expect the CARB-X awards to partially fund the forecasted expenses for the development of ETX0282 through Phase 1 clinical development and the forecasted expenses for our NBP program from lead-optimization through Phase 1 clinical trials for an initial clinical candidate. The funding from the U.S. Department of Defense is structured as a single, $1.1 million award and supports the development of anti-infective agents to combat Gram-negative bacteria.

NIAID fully funded the Phase 2 clinical trial of zoliflodacin for the treatment of uncomplicated gonorrhea and has provided funding commitments for the Phase 3 clinical trial preparatory activities, including the granule formulation bioequivalence Phase 1 trial and the TQT cardiovascular clinical trial.

Commercial Agreements

Business Transfer and Subscription Agreement with AstraZeneca

In May 2015, we entered into a Business Transfer and Subscription Agreement, or the AstraZeneca Agreement, with AstraZeneca, AstraZeneca UK Limited and AstraZeneca Pharmaceuticals LP, which was amended and restated in March 2016 and further amended in August 2017, pursuant to which we obtained, among other things, worldwide rights to ETX2514, ETX0282 and zoliflodacin.

Pursuant to the terms of the AstraZeneca Agreement, we sold 33,499,900 A preference shares to AstraZeneca in consideration for property and equipment, clinical materials, intellectual property and net cash proceeds of $23.3 million. Pursuant to our corporate reorganization, the A preference shares were exchanged for Series A preferred stock. The Series A preferred stock was automatically converted into 1,616,166 shares of our common stock upon completion of our IPO. We also agreed to pay AstraZeneca a one-time milestone payment of $5.0 million within three months of achieving a specified cumulative net sales milestone for ETX2514. This milestone payment will be automatically waived should our common stock trade on Nasdaq at or above a specified price at the time we achieve such specified cumulative net sales milestone for ETX2514, subject to adjustment for share splits, dividends and other similar events. We are also obligated to pay AstraZeneca a one-time milestone payment of $10.0 million within two years of achieving the first commercial sale of zoliflodacin. Following the achievement of either milestone, we are not permitted to pay dividends or make other distributions to any of our stockholders until the applicable milestone payment has been paid in full. If our board of directors deems the milestone payment obligation related to zoliflodacin to be significantly burdensome, AstraZeneca is required to explore in good faith modifications to the timing of such payment. At our election, either milestone payment may be paid in cash, shares of our common stock, or a combination of cash and stock. Additionally, we are obligated to pay AstraZeneca tiered, single-digit royalties on the annual worldwide net sales of ETX2514 and, and the lesser of tiered, single-digit royalties on the worldwide annual net sales of zoliflodacin and a specified share of the royalties we receive from sublicensees of zoliflodacin. Royalties on sales of zoliflodacin do not include sales by GARDP in low-income and specified middle-income countries as discussed below. Our obligation to make these royalty payments expires with respect to each product on a country-by-country basis upon the later of (i) the 10 year anniversary of the first commercial sale of a product in each such country or (ii) when the last patent right covering a product expires

in each such country. We are required to use diligent efforts to achieve the first commercial sale of zoliflodacin and to commercialize, market, promote and sell zoliflodacin and ETX2514.

Under the AstraZeneca Agreement, we granted AstraZeneca a non-exclusive, non-transferrable license to use the transferred intellectual property solely for internal research and development purposes unrelated to the field of small molecule anti-infectives.

Collaboration Agreement with GARDP

In July 2017, we entered into a collaboration agreement with GARDP for the development and commercialization of a product candidate containing zoliflodacin in certain countries. Under the terms of the collaboration agreement, GARDP will use commercially reasonable endeavors to perform and fully fund the Phase 3 clinical trial, including the manufacture and supply of the product candidate containing zoliflodacin, in uncomplicated gonorrhea. We are obligated to use commercially reasonable efforts to conduct and fund a TQT study on the granule formulation of zoliflodacin in collaboration with NIAID, which has been fully enrolled. We are also obligated to commit reasonably sufficient time and resources to collaborate in the design of the Phase 3 clinical trial and the development of the protocol for the trial and to provide know-how relating to zoliflodacin and any future product candidate. We estimate that we will incur annual expenses of approximately $120,000 related to ongoing costs for active pharmaceutical ingredient stability, drug product storage, intellectual property maintenance and travel. Both parties are responsible for obtaining marketing authorizations for any future product candidate in such parts of their respective territories as they elect.

In addition, under the collaboration agreement, we have granted GARDP a worldwide, fully paid, exclusive and royalty-free license, with the right to sublicense, to use our zoliflodacin technology in connection with GARDP's development, manufacture and commercialization of zoliflodacin in low-income and specified middle-income countries, which we refer to collectively as the GARDP territory. We have retained commercial rights in all other countries worldwide, including the major markets in North America, Europe and Asia-Pacific. We also have retained the right to use and grant licenses to our zoliflodacin technology to perform our obligations under the collaboration agreement and for any purpose other than gonorrhea or community-acquired indications. GARDP will own all intellectual property developed in its performance under the collaboration agreement regarding formulation development of zoliflodacin. To the extent GARDP does not file patent applications for any such technology it develops under this collaboration agreement within six months of making or conceiving any invention related to such technology or does not use reasonable efforts to prosecute such patent applications and maintain such patents, GARDP shall assign to us the rights to such intellectual property. In the event we undertake and fund additional efforts outside of the current agreed-upon development plan for zoliflodacin in our territory that lead to the creation of new intellectual property, we will have a right to file and maintain this new intellectual property. In addition, we are obligated to maintain the intellectual property in the countries in the GARDP territory where we filed patent rights at the date of the agreement and, under specified conditions, in our territory, and GARDP must reimburse us for costs and expenses for the maintenance of such intellectual property rights in the countries of the GARDP territory. If we believe the results of the planned Phase 3 clinical trial of zoliflodacin would be supportive of an application for marketing approval, we are obligated to use our best efforts to file an application for marketing approval with the FDA within six months of the completion of the trial and to use commercially reasonable endeavors to file an application for marketing approval with the EMA. Each party is responsible for using commercially reasonable efforts to obtain marketing authorizations for the product candidate in their respective territories.

Both parties have the right to terminate the collaboration agreement with 90 days' written notice if the other party is in material breach or remains in material breach after a cure period, or with immediate effect upon the occurrence of certain specified events of insolvency. The collaboration agreement may also be terminated upon mutual written agreement. Either party may terminate the collaboration agreement at any time after completion or earlier termination of the Phase 3 clinical trial with 12 months' prior notice. We may terminate the collaboration agreement if GARDP has not achieved certain clinical milestones within a specified time period, unless the nonachievement was due to specified types of delay.

License and Collaboration Agreement with Zai Lab

In April 2018, we entered into a license and collaboration agreement with Zai Lab for the development and commercialization of products containing ETX2514 or ETX2514SUL in the following countries in the Asia Pacific region: China, Hong Kong, Macau, Taiwan, Korea, Vietnam, Thailand, Cambodia, Laos, Malaysia, Indonesia, the Philippines, Singapore, Australia, New Zealand and Japan, which we refer to collectively as the territory. Under the agreement, we granted Zai Lab an exclusive, royalty-bearing license, with the right to sublicense, under our technology to develop, manufacture and sell products containing ETX2514 or ETX2514SUL, or the licensed products, in the territory. Additionally, we granted Zai Lab a non-exclusive, worldwide license to our technology as required for Zai Lab to practice its exclusive license with respect to the licensed products. We retain the right to use our technology to perform our obligations under the agreement and retain the exclusive right to use our technology in all other countries, including North America and Europe.

Under the agreement, Zai Lab will use commercially reasonable efforts to perform and fund costs associated with our planned Phase 3 clinical trial of ETX2514SUL in China. Zai Lab is responsible, at its expense, for developing licensed products in the territory, to be coordinated with our continued global efforts with respect to products containing ETX2514SUL. Zai Lab must use commercially reasonable efforts to conduct development activities described in the agreed-upon written development plan and to obtain regulatory approval in a specified number of countries in the territory beyond China after regulatory approval of a licensed product in China. Zai Lab is also solely responsible for commercializing licensed products in the territory and must use commercially reasonable efforts to commercialize licensed products for which it has obtained regulatory approval. We are obligated to use commercially reasonable efforts to conduct specified development obligations delegated to us pursuant to the agreed-upon development plan for the territory. We are also obligated to supply Zai Lab with the licensed products for clinical development, although Zai Lab may take over manufacturing responsibilities for its own commercialization activities within a specified time period following the effective date of the agreement. Both parties are prohibited from developing and commercializing products in the territory that would compete with the licensed products.

In addition, under the agreement, either party may propose that Zai Lab pursue a combination of imipenem together with ETX2514SUL in the territory. If the parties decide to pursue an imipenem combination, Zai Lab would provide us with limited research and development support for the combination.

We received an upfront payment of $5.0 million and $300,000 in research support, less applicable taxes, from Zai Lab in 2018. We are eligible to receive up to an aggregate of $98.3 million in additional research and development support payments and development, regulatory and sales milestone payments related to ETX2514SUL, imipenem and other combinations with the licensed products. In the event the China Food and Drug Administration requires a modification or supplement to the trial protocol, and we delay Zai Lab from providing the required information and subsequently from obtaining regulatory approval for the pivotal study of ETX2514SUL in China, then the sales-based milestone payments that become due to us will be reduced by an agreed amount that increases with the length of the delay. Zai Lab will pay us a tiered royalty equal to a high-single digit to low-double digit percentage based on annual net sales of licensed products in the territory, subject to specified reductions for the market entry of competing products, loss of patent coverage of licensed products and for payments owed to third parties for additional rights necessary to commercialize licensed products in the territory.

Each party will own any inventions made by it, and jointly made inventions will be jointly owned, but we will own any inventions that relate to the composition of matter or method of use of licensed products regardless of the party that makes the invention. We will control the prosecution and maintenance of the licensed patents, but Zai Lab will have the ability to take over such prosecution and maintenance if we fail to do so. Zai Lab will have the first right to control any legal action with respect to third-party infringement of the product in the territory, but we may take over such action if Zai Lab fails to act.

Zai Lab may terminate the agreement upon written notice to us at any time and for any reason. Either party may terminate the agreement if the other party is in material breach after a permitted cure period, or with immediate effect upon the occurrence of specified events of insolvency. Further, we can terminate the agreement if Zai Lab ceases to commercialize the licensed products or challenges any of the patents we licensed to it. If Zai Lab has the right to

terminate the agreement due to our uncured material breach, Zai Lab may elect to continue the agreement and we would be obligated to pay Zai Lab a premium on the amount of damages arising from such breach. In the event of any termination of the agreement, Zai Lab will assign or grant a right of reference to any regulatory documentation related to the licensed products to us, all rights and licenses to Zai Lab will terminate, and Zai Lab will grant us a license under Zai Lab's technology to make and commercialize licensed products in the territory.

Competition

The biopharmaceutical industry is very competitive and subject to rapid innovation. Our potential competitors include major multinational pharmaceutical companies, biotechnology companies, specialty pharmaceutical companies and generic drug companies. Many of our 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. Consequently, these companies may prove more successful in obtaining regulatory approval and in selling and marketing their products. We anticipate intense competition as new drugs enter the market. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our product candidates obsolete or noncompetitive before we can recover the expenses of their development commercialization.

We are initially developing ETX2514SUL for the treatment of multidrug-resistant *Acinetobacter* infections. Due to rising resistance rates, standard-of-care treatment for multidrug-resistant *Acinetobacter* often includes a combination of several last-line treatment options, including carbapenems, tetracyclines and polymyxins, all generically available agents. We are aware of other potentially competitive products or product candidates in clinical development that have shown *in vitro* activity against *Acinetobacter*: minocycline, marketed by Melinta Therapeutics Inc., eravacycline, recently approved for complicated intra-abdominal infections, and TP6076, currently in a Phase 1 clinical trial, from Tetraphase Pharmaceuticals, Inc. and cefiderocol, currently in a Phase 3 clinical trial, from Shionogi & Co., Ltd.

We are initially developing zoliflodacin for the treatment of gonorrhea. Gonorrhea is commonly treated with combination therapy intramuscular ceftriaxone injection and oral azithromycin, both generically available agents. Additional generic cephalosporins and fluoroquinolones are also prescribed, but not recommended as primary treatment options given current resistance rates. Gepotidacin, currently under development for a variety of infections by GlaxoSmithKline plc, is the only potentially competitive product candidate in clinical development that we are aware of that is being developed for the treatment of gonorrhea.

We are initially developing ETX0282CPDP for the treatment of complicated UTIs. There are a variety of generically available antibiotic classes available for the treatment of such infections, including cephalosporins, carbapenems and fluoroquinolones. Additionally, there are several recently approved and likely to be approved branded agents targeting multidrug-resistant complicated UTIs, including Avycaz, Vabomere and Zemdri™. We are aware of additional potentially competitive oral product candidates in clinical development that may address a limited breadth of multidrug-resistant Gram-negative pathogens: sulopenem from Iterum Therapeutics Limited, currently in a Phase 3 clinical trial, C-Scape from Achaogen, Inc., currently in a Phase 1 clinical trial, and tebipenem from Spero Therapeutics Inc., currently in a Phase 1 clinical trial.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our product candidates, our core technologies, and other know-how, to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary or intellectual property rights. Our policy is to seek to protect our proprietary and intellectual property position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how that is not patentable, we rely on trade secret protection and confidentiality agreements to protect our interests. We require our employees, consultants and advisors to enter into confidentiality agreements prohibiting the

disclosure of confidential information and requiring disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

We file patent applications directed to our key product candidates to establish intellectual property positions. These patent applications are intended to protect new chemical entities relating to these product candidates as well as their manufacturing processes, intermediates and uses in the treatment of diseases.

The intellectual property portfolios for our most advanced product candidates are summarized below.

ETX2514

Our intellectual property portfolio for our ETX2514 program contains patent applications directed to compositions of matter for ETX2514 and other chemical analogs, as well as methods of making, referred to as synthetic methods, and methods of use and modes of treatment using ETX2514 in combination with one or more antibiotic compounds. As of December 31, 2018, we owned three issued U.S. patents, 53 issued foreign patents as well as 27 pending foreign patent applications. The issued foreign patents are in several jurisdictions including Australia, the European Union, China, Israel, India, Japan, Mexico, New Zealand, Philippines, Russia, Singapore, South Africa and Taiwan. Issued U.S. and foreign patents and patents issuing from pending U.S. and foreign applications will have expiration dates of April 2033 and November 2035.

Zoliflodacin

Our intellectual property portfolio for zoliflodacin contains patent applications directed to compositions of matter for zoliflodacin and other chemical analogs as well as synthetic methods and methods of use and modes of treatment. As of December 31, 2018, we owned six issued U.S. patents, 19 issued foreign patents as well as 34 pending foreign patent applications. The issued foreign patents are in several jurisdictions, including Australia, Canada, China, Eurasia, the European Union, Hong Kong, Japan, Mexico, New Zealand, Singapore, South Africa, South Korea and Taiwan. Issued U.S. and foreign patents and patents issuing from pending U.S. and foreign applications have expiration dates of October 2029, January 2034 and May 2035.

ETX0282

Our intellectual property portfolio for our ETX0282 program contains patent applications directed to compositions of matter for the prodrug ETX0282, the active molecule, ETX1317, and other chemical analogs, as well as methods of making them, referred to as synthetic methods, and methods of use and modes of treatment using ETX0282 and ETX1317 in combination with one or more antibiotic compounds. As of December 31, 2018, we owned one pending foreign patent application in Taiwan and one published PCT. Issued U.S. and foreign patents and patents issuing from pending U.S. and foreign applications will have expiration dates of September 2037.

Provisional Patents

In addition to the issued and pending patent applications covering our most advanced product candidates, our portfolio also includes one pending foreign patent application in Taiwan and two published PCT applications relating to our early stage discovery projects.

Patent Term and 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 twenty years from the earliest effective 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 U.S. Patent and Trademark Office, or the USPTO, 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 or biological product may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The Drug Price Competition and

Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date of a U.S. patent as partial compensation for the length of time the drug is under regulatory review while the patent is in force. A patent term extension cannot extend the remaining term of a patent beyond a total of fourteen years from the date of product approval, only one patent applicable to each regulatory review period 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 cannot provide any assurance that any patent term extension with respect to any U.S. patent will be obtained and, if obtained, the duration of such extension.

Similar provisions are available in the European Union and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors. The expiration dates referred to above are without regard to a potential patent term extension or another market exclusivity that may be available to us. However, we cannot provide any assurances that any such patent term extension of a foreign patent will be obtained and, if obtained, the duration of such extension.

Our patents and patent applications are subject to procedural or legal challenges by others. We may be unable to obtain, maintain and protect the intellectual property rights necessary to conduct our business, and we may be subject to claims that we infringe or otherwise violate the intellectual property rights of others, which could materially harm our business. For more information, see the section titled “Risk Factors—Risks Related to Our Intellectual Property.”

Intellectual Property from the Collaboration with GARDP

In July 2017, we entered into a collaboration agreement with GARDP for the development and commercialization of a product candidate containing zoliflodacin in certain countries. GARDP will own all intellectual property developed in its performance under the collaboration agreement regarding formulation development of zoliflodacin. To the extent GARDP does not file patent applications for any such technology it develops under this collaboration agreement within six months of making or conceiving any invention related to such technology or does not use reasonable efforts to prosecute such patent applications and maintain such patents, GARDP is obligated to assign to us the rights to such intellectual property. In the event we undertake and fund additional efforts outside of the current agreed-upon development plan for zoliflodacin in our territory that lead to the creation of new intellectual property, we will have a right to file and maintain this new intellectual property. In addition, we are obligated to maintain the intellectual property in the countries in the GARDP territory where we had patents or had filed patent applications prior to the agreement and, under specified conditions, in our territory, and GARDP must reimburse us for costs and expenses for the maintenance of such intellectual property rights in the countries of the GARDP territory.

Trademarks, Trade Secrets and Know-How

Our trademark portfolio currently consists of registered trademark and service mark rights for ENTASIS THERAPEUTICS in several jurisdictions, including the United States, the European Union, Japan, Argentina, Australia, Brazil, Canada, India, Norway, the Russian Federation, Switzerland and Taiwan, and pending applications in other jurisdictions. In addition, we have registered trademark rights for ENTASIS THERAPEUTICS (plus design) in the European Union. In connection with the ongoing development and advancement of our products and services in the United States and various international jurisdictions, we routinely seek to create protection for our marks and enhance their value by pursuing trademarks and service marks where available and when appropriate. In addition to patents and trademark protection, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees, and consultants, and invention assignment agreements with our employees. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners, collaborators, employees, and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Government Regulation

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, testing, manufacture, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, import and export of pharmaceutical products. In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. To market any product outside of the United States, a sponsor must comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product candidate, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Review and Approval of New Drug Products in the United States

In the United States, the process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local statutes and regulations requires the expenditure of substantial time and financial resources. The failure to comply with the applicable 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 applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and untitled letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil 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 the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or 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, or GCP, to establish the safety and efficacy of the proposed drug for each indication;
- submission to the FDA of a new drug application, or NDA;
- review of the proposed product by an FDA advisory committee, where appropriate;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;

- FDA review and approval of the NDA; and

- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA.

Preclinical Studies and IND

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial. In support of a request for an IND, an applicant must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as in vitro and animal studies to assess the potential for adverse events, and in some cases, to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue 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 trial on 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. 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.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements of the FDA must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA to use the study as support for an IND or application for marketing approval. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety 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, and the IRB must conduct continuing review. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations.

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.

- *Phase 2:* The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase 3:* The drug is administered to an expanded patient population in adequate and well controlled clinical trials to generate sufficient data to statistically confirm 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.

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. 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.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee or DSMB. This group provides authorization for whether a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination at www.clinicaltrials.gov.

Combination Rule

The FDA's Combination Rule governing fixed combination drug products provides that two or more drugs may be combined in a single dosage form when each component contributes to the claimed effects and the dosage of each component (amount, frequency, duration) is such that the combination is safe and effective for a significant patient population requiring such concurrent therapy as defined in the labeling for the drug. The Rule is meant to ensure that any fixed-dose combination drug provides an advantage to the patient over and above that obtained when one of the individual ingredients is used in the usual safe and effective dose.

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. Under federal law, the submission of most NDAs is subject to an application user fee, and the sponsor of an approved NDA is also subject to an annual program fee. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses.

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 a 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 has agreed to specified performance goals in the review of NDAs. Under these goals, the FDA has committed to review most such applications for nonpriority products within 10 months from filing, and most applications for priority review products, that is, drugs that the FDA determines represent a significant improvement over existing therapy, within six months from filing. The

review process may be extended by the FDA for three additional months to consider certain information or clarification regarding information already provided in the submission.

The FDA may also refer applications for novel drugs or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. 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. Under the FDCA, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain drug applications, including applications for drugs in a shortage or drugs for which approval is dependent on remediation of conditions identified in the inspection report. In addition, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and integrity of the clinical data submitted.

The FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, 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.

After the FDA's evaluation of the NDA and inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes the commercial marketing of the drug with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval and refuse to approve the NDA.

Even if the FDA approves a product, it may limit the approved indications for use for 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 restrictions or other risk management mechanisms, including Risk Evaluation and Mitigation Strategies, or 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-market 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.

Fast Track Designation

The FDA is required to facilitate the development and expedite the review of drugs that are intended for the treatment of a serious or life-threatening condition for which there is no effective treatment, and which demonstrate the potential to address unmet medical needs for the condition. Under the Fast Track program, the sponsor of a new product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the submission of the IND for the product candidate. The FDA must determine if the product candidate qualifies for Fast Track designation within 60 days after receipt of the sponsor's request.

For Fast Track products, the sponsor may have more frequent interactions with the FDA and the FDA may initiate a review of sections of a Fast Track product's NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and

the applicant pays applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the NDA is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process. A Fast Track designated product candidate would ordinarily meet the FDA's criteria for priority review.

Accelerated Approval

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval trials or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Breakthrough Therapy Designation

A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Section 505(b)(2) NDAs

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

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with the passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the

statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. For an ANDA to be approved, the FDA must find that the generic version is identical to the Reference Listed Drug, or RLD, with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. The FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug..."

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication Approved Drug Products with Therapeutic Equivalence Evaluations, also referred to as the Orange Book. Clinicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in the substitution of the generic drug without the knowledge or consent of either the prescribing clinicians or patient.

The FDA may not approve an ANDA until any applicable period of nonpatent exclusivity for the RLD has expired. The FDCA provides a period of five years of nonpatent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of "competitor generic therapies" or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage to, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication.

During the seven year exclusivity period, the FDA may not approve any other applications to market the same drug for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity in that it is shown to have greater efficacy or safety, makes a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

Qualified Infectious Disease Products

In response to the growing unmet medical need in the area of serious bacterial infections, the Generating Antibiotic Incentives Now Act, or the GAIN Act, provides incentives including access to expedited FDA review for approval and five years of potential market exclusivity extension, for the development of new, qualified infectious disease products, or QIDP, including antibacterial or antifungal drugs intended to treat serious or life-threatening

infections that are resistant to treatment, or that treat qualifying resistant pathogens identified by the FDA. A sponsor must request QIDP designation for a new drug before an NDA is submitted and, if designated as a QIDP and approved, is eligible for an additional five years of exclusivity beyond any period of exclusivity to which it would have otherwise been entitled. In addition, a QIDP receives NDA priority review and Fast Track designation. QIDP designation does not affect the likelihood of approval by FDA.

Pediatric Exclusivity and Pediatric Use

The Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for most drugs and biologics, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, biologics license applications and supplements thereto, must contain a pediatric assessment unless the sponsor has received a deferral or waiver. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which an orphan drug designation has been granted. The required assessment must assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin.

Pediatric exclusivity is another type of nonpatent 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 nonpatent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do 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.

Post-Approval Regulatory Requirements

Any drug manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval.

The FDA may impose several post-approval requirements, 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 us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain cGMP compliance.

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 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 include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- consent decrees, injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, healthcare professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the U.S. Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementation regulations, as well as the Drug Supply Chain Security Act, or DSCSA, which regulates the distribution of and tracing of prescription drugs and prescription drug samples at the federal level and sets minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCSA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all the approved products for a particular indication.

To secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies to demonstrate the medical necessity and cost effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. Additionally, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the

drug product. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

Health Care Laws Governing Interactions with Healthcare Providers

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws restrict our business activities, including certain marketing practices. These laws include, without limitation, anti-kickback laws, false claims laws, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item, good, facility or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers, among others, on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration that are alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the federal Anti-Kickback Statute has been violated. Additionally, the intent standard under the federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the Affordable Care Act, or ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

Federal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly inflating drug prices they report to pricing services, which in turn were 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.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal and civil statutes that prohibit among other actions, knowingly and willfully 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 knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the federal Anti-Kickback Statute, the ACA amended the intent standard for certain healthcare fraud under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it to have committed a violation.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, impose certain requirements on covered entities (i.e., certain healthcare providers, health plans and healthcare clearinghouses) relating to the privacy, security and

transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four 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 federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.

Additionally, the federal Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, require certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to annually report information related to certain payments or other transfers of value provided to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and information related to certain ownership and investment interests held by physicians and their immediate family members.

Finally, the majority of states also have statutes or regulations similar to the aforementioned federal laws, some of which are broader in scope and apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government. In addition, some state laws require drug manufacturers to report information related to payments to clinicians and other healthcare providers or marketing expenditures and drug pricing. Further, some state and local laws require the licensure of pharmaceutical sales representatives. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform Efforts

A primary trend in the United States healthcare industry and elsewhere is cost containment. Over the last several years, there have been federal and state proposals and legislation enacted regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, and making changes to healthcare financing and the delivery of care in the United States.

In March 2010, the ACA was enacted, which includes measures that have significantly changed health care financing by both governmental and private insurers. The provisions of the ACA of importance to the pharmaceutical and biotechnology industry are, among others, the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drug agents or biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts to 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;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;

- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- 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 certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and 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;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of any certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or the Tax Act, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high-cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on nonexempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, 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." In July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace ACA will impact ACA.

In addition, other federal health reform measures have been proposed and adopted in the United States since the ACA was enacted. For example, because of the Budget Control Act of 2011, as amended by subsequent legislation including the BBA, providers are subject to Medicare payment reductions of 2% per fiscal year through 2027 unless additional Congressional action is taken. Further, the American Taxpayer Relief Act of 2012 reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments from providers from three to five years. The Medicare Access and CHIP Reauthorization Act of 2015 also introduced a quality payment program under which certain individual Medicare providers will be subject to certain incentives or penalties based on new program quality standards. Payment adjustments for the Medicare quality payment program will

begin in 2019. At this time, it is unclear how the introduction of the quality payment program will impact overall physician reimbursement under the Medicare program.

Further, there has been heightened governmental scrutiny over the way manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and enacted federal and state legislation proposed designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. The Trump administration also released a "Blueprint", or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug 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. On January 31, 2019, the Department of Health and Human Services, Office of Inspector General, proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations. While some of these and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

At the state level, legislatures have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare 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 healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or the FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts.

Review and Approval of New Drug Products in the European Union

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of an EU member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial applications must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a product under EU regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the European Medicines Agency, or EMA, is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, by when additional information or written or oral explanation must be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and from the viewpoint of therapeutic innovation. In these circumstances, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various EU member states where such product has not previously received marketing approval in any EU member states before. The decentralized procedure provides for approval by one or more other member states (known as concerned member states) of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may, eventually, be referred to the European Commission, whose decision is binding on all member states.

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

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

Clinical Trial Approval in the European Union

Requirements for the conduct of clinical trials in the European Union, including Good Clinical Practice, or GCP, are set forth in the Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. Pursuant to Directive 2001/20/EC and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union

has been implemented through national legislation of the EU member states. Under this system, approval must be obtained from the competent national authority of each EU member state in which a study is planned to be conducted. To this end, a CTA is submitted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and other applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

In April 2014, the European Union passed the new Clinical Trials Regulation, (EU) No 536/2014, which will replace the current Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the European Union, the new EU clinical trials legislation was passed as a regulation that is directly applicable in all EU member states. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (EU) No 536/2014 becomes applicable. According to the current plans of the EMA, the new Clinical Trials Regulation will become applicable in 2019. The Clinical Trials Directive 2001/20/EC will, however, still apply three years from the date of entry into application of the Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for old system.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trial in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the EU portal; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states; a harmonized procedure for the assessment of applications for clinical trials, which is divided into two parts (Part I is assessed jointly by all member states concerned, and Part II is assessed separately by each member state concerned); strictly defined deadlines for the assessment of clinical trial applications; and the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Clinical Trials Regulation.

Periods of Authorization and Renewals

A marketing authorization is valid for five years in principle and may be renewed after five years based on a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the EU market (in case of centralized procedure) or on the market of the authorizing member state (in the case of the decentralized procedure) within three years after authorization ceases to be valid (the so-called sunset clause).

Data and Market Exclusivity in the European Union

In the European Union, new chemical entities qualify for eight years of data exclusivity upon the grant of a marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which a generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company can complete a full MAA with a complete database of pharmaceutical test, preclinical tests and clinical trials and obtain marketing approval of its product.

Orphan Drug Designation and Exclusivity

Regulation 141/2000 provides that a drug shall be designated as an orphan drug if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Community when the application is made, or that the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Community and that without incentives it is unlikely that the marketing of the drug in the European Community would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Community or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Regulation 847/2000 sets out criteria and procedures governing designation of orphan drugs in the European Union. Specifically, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a 10year period of market exclusivity. This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, for example, because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of "clinically relevant superiority" by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply). Medicinal products designated as orphan drugs pursuant to Regulation 141/2000 shall be eligible for incentives made available by the European Community and by the member states to support research into, and the development and availability of, orphan drugs.

Regulatory Requirements after Marketing Authorization

As in the United States, both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU member states both before and after grant of the manufacturing and marketing authorizations. The holder of an EU marketing authorization for a medicinal product must, for example, comply with EU pharmacovigilance legislation and its related regulations and guidelines which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. The manufacturing process for medicinal products in the European Union is also highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, including compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients.

In the European Union, the advertising and promotion of approved products are subject to EU member states' laws governing promotion of medicinal products, interactions with clinicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU member states may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does SmPC is considered to constitute off-label promotion, in the European Union.

Corporate and Other Information

Entasis Therapeutics Holdings Inc. was incorporated under the laws of the State of Delaware in March 2018. Our shares are listed on the NASDAQ Global Market, where our trading symbol is ETTX. Our principal executive offices are located at 35 Gatehouse Drive, Waltham, Massachusetts 02451 and our telephone number is (781) 810-0120.

As of March 15, 2019, we had 33 full-time employees, all of whom were located in the United States and employed by our U.S. subsidiary, Entasis Therapeutics Inc. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

We have three subsidiaries: Entasis Therapeutics Limited, which was incorporated under the laws of England and Wales on March 6, 2015; Entasis Therapeutics Inc., which was incorporated under the laws of the State of Delaware on March 11, 2015; and Entasis Therapeutics Security Corporation, which was incorporated under the laws of the State of Massachusetts on October 31, 2018.

Available Information

You may read our SEC filings, including our proxy statements, annual reports 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 Section 13(a) or 15(d) of the Exchange Act, over the internet at the SEC's website at *www.sec.gov*. We also maintain a website at *www.entasistx.com*, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this Annual Report.

Item 1A. Risk Factors

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Annual Report on Form 10-K, including our financial statements and related notes hereto, before deciding to invest in our common stock. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. In these circumstances, the market price of our common stock could decline; and you may lose all or part of your investment.

Risks Related to Our Financial Position and Capital Needs

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

We are a clinical-stage biopharmaceutical company with a limited operating history. We have not generated any revenue from the sale of products and have incurred losses in each year since our inception in 2015. Our net loss was $33.0 million and $29.9 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an accumulated deficit of $90.1 million. We have funded our operations to date primarily with proceeds from the sale of convertible preferred stock in private placements and the sale of common stock in our initial public offering. We have also either directly received funding or financial commitments from, or have had our program activities conducted and funded by, the U.S. government through our arrangements with the U.S. National Institute of Allergy and Infectious Diseases, or NIAID, the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program, or CARB-X, and the U.S. Department of Defense, and have received non-profit awards from the Global Antibiotic Research and Development Partnership, or GARDP, and an upfront payment of $5.0 million and research support funding of $0.3 million, less applicable taxes, from our license and collaboration agreement with Zai Lab (Shanghai), Co., Ltd., or Zai Lab.

We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials. We are still in the early stages of development of our product candidates, and we have not completed development of any drugs. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- continue our ongoing and planned preclinical and clinical development of our product candidates;
- initiate preclinical studies and clinical trials for any additional product candidates that we may pursue in the future;
- seek to discover and develop additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- ultimately establish sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any product candidate for which we may obtain regulatory approval and intend to commercialize on our own;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, scientific, and chemistry, manufacturing and controls personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and

- incur additional legal, accounting and other expenses associated with operating as a public company.

To become and remain profitable, we and our collaborators must succeed in developing and eventually commercializing drugs that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates and preclinical program, obtaining regulatory approval, manufacturing, marketing and selling any products for which we may obtain regulatory approval, as well as discovering and developing additional product candidates. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we are required by regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in the initiation and completion of our clinical trials or the development of any of our product candidates, our expenses could increase.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our common stock and could impair our ability to raise capital, expand our business, maintain our research and development efforts or continue our operations. A decline in the value of our common stock could also cause you to lose all or part of your investment.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced active operations in 2015, and our operations to date have been largely focused on raising capital, identifying and developing our product candidates and preclinical program, broadening our expertise in the development of our product candidates, and undertaking preclinical studies and conducting early-stage clinical trials. As an organization, we have not yet demonstrated an ability to successfully complete Phase 3 clinical trials, obtain regulatory approvals, 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 commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We require substantial additional funding to meet our financial needs and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to delay, reduce or altogether cease our product development programs or commercialization efforts.

We believe that the net proceeds from our initial public offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2020, which is at least 12 months from the date the financial statements included in this report were issued. However, we will need to obtain substantial additional funding in connection with our continuing operations and planned activities. Our future capital requirements will depend on many factors, including:

- the timing, progress and results of our ongoing clinical trials of our product candidates;

- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials of other product candidates that we may pursue;

- the number and development requirements of other product candidates that we may pursue;
- the amount of funding that we receive under our government awards and government awards that we have applied for;
- our ability to establish collaborations on favorable terms, if at all;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the costs of operating as a public company; and
- the extent to which we acquire or in-license other product candidates and technologies.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or altogether cease our research and development programs or future commercialization efforts.

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaboration, license and development agreements and government/non-profit grants and awards. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. 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.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to 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 drug development or future commercialization efforts or grant rights to a third party to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2018, we had U.S. federal, state and foreign net operating loss carryforwards, or NOLs, of $33.8 million, $34.5 million and $63.3 million, respectively. Our pre-2018 U.S. NOLs begin to expire in 2035. Under the newly enacted Tax Cuts and Jobs Act, U.S. federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various U.S. states will conform to the Tax Cuts and Jobs Act. To the extent that we continue to generate taxable losses in the United States, unused losses will carry forward to offset future taxable income (subject to any applicable limitations), if any, until such unused losses expire. Under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes to offset its post-change U.S. federal income or U.S. federal taxes may be limited. We may have experienced ownership changes in the past and may experience ownership changes in the future and/or subsequent shifts in our share ownership (some of which shifts are outside our control). As a result, if we earn net taxable income for U.S. federal income tax purposes, our ability to use our pre-change NOLs to offset such taxable income may be subject to limitations. Similar provisions of U.S. state tax law may also apply to limit our use of accumulated state tax attributes, including our state NOLs. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes, which could negatively impact our future cash flows.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, the Internal Revenue Service or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. The foregoing are only selected examples of potential challenges, and other tax positions we have taken or may take in the future could become the subject of disputes with one or more tax authorities. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Risks Related to the Development of Our Product Candidates and Preclinical Program

We depend to a large degree on the success of our most advanced product candidates, which are in clinical development but have not completed Phase 3 clinical trials. If we do not obtain regulatory approval for and successfully commercialize one or more of our product candidates or if we experience significant delays in doing so, we may never become profitable.

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources on the development of ETX2514SUL and ETX0282CPDP as product candidates for the treatment of serious infections caused by multidrug-resistant Gram-negative bacteria. We expect that a substantial portion of our efforts and expenses over the next few years will be devoted to the development of ETX2514SUL, ETX0282CPDP and any other product candidates we develop. As a result, our business currently depends heavily on the successful development, regulatory approval and, if approved, commercialization of ETX2514SUL, zoliflodacin, ETX0282CPDP and any other product candidates we develop. We cannot be certain that our product candidates will receive regulatory approval or will be successfully commercialized even if they receive regulatory approval. The research, development, manufacturing, safety, efficacy, labeling, approval, sale, marketing and distribution of our product candidates are, and will remain, subject to comprehensive regulation by the U.S. Food and Drug Administration, or FDA, the European

Medicines Agency, or EMA, and comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through preclinical studies and clinical trials that the product candidate is safe and effective for use in each target indication. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical trials. Failure to obtain regulatory approval for our product candidates in the United States will prevent us from commercializing and marketing our product candidates. The success of our product candidates and preclinical program will depend on several additional factors, including:

- successful completion of preclinical studies and requisite clinical trials;
- performing preclinical studies and clinical trials in compliance with the FDA, the EMA or any comparable regulatory authority requirements;
- receipt of marketing approvals from applicable regulatory authorities;
- the ability of collaborators to manufacture sufficient quantity of product for development, clinical trials or potential commercialization;
- obtaining marketing approvals with labeling for sufficiently broad patient populations and indications, without unduly restrictive distribution limitations or safety warnings, such as black box warnings or a Risk Evaluation and Mitigation Strategies, or REMS, program;
- obtaining and maintaining patent, trademark and trade secret protection, and regulatory exclusivity for our product candidates and preclinical program;
- making arrangements with third-parties for manufacturing capabilities;
- launching commercial sales of products, if and when approved, whether alone or in collaboration with others;
- acceptance of the therapies, if and when approved, by physicians, patients and third-party payors;
- competing effectively with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- protecting our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of our drugs following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would harm our business.

We may not be successful in our efforts to build a pipeline of product candidates.

A key element of our strategy is to build a pipeline of product candidates and to progress these product candidates through clinical development for the treatment of serious infections caused by multidrug-resistant Gram-negative bacteria. We may not be able to develop product candidates that are safe and effective. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including because of significant safety, tolerability or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval, achieve market acceptance or obtain reimbursements from third-party payors. If we do not successfully develop and commercialize product candidates or collaborate with others to

do so, we will not be able to obtain product revenue in future periods, which could significantly harm our financial position and adversely affect the trading price of our common stock.

Success in preclinical studies or clinical trials may not be indicative of results in future clinical trials.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials. For instance, with respect to ETX2514SUL, we cannot guarantee that the dose regimen used in the Phase 3 clinical trial will be effective. We cannot guarantee that the rigorous pharmacokinetic and pharmacodynamic modeling approach, including input from the completed Phase 1 clinical trial assessing pharmacokinetics in renally impaired patients and the completed Phase 2 clinical trial in patients with complicated urinary tract infections, or UTIs, that we will use to select the Phase 3 dosing regimen will be validated in the Phase 3 clinical trial in patients with *Acinetobacter* infections. The dose regimen to be used in the single Phase 3 clinical trial will be the first evaluation of ETX2514SUL in patients with pneumonia and bloodstream infections caused by *Acinetobacter*. Our observation of ETX2514SUL penetration into the lung in the Phase 1 clinical trial may not be predictive of efficacy in pneumonia caused by *Acinetobacter*.

In addition, the design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. As an organization, we have limited experience designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. There is a high failure rate for drugs and biologic products proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections because of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

If clinical trials of ETX2514SUL, zoliflodacin, ETX0282CPDP or any other product candidate that we may advance to clinical trials fail to demonstrate safety and efficacy to the satisfaction of the FDA, the EMA or other comparable 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 ETX2514SUL, zoliflodacin, ETX0282CPDP or any other product candidate.

We may not commercialize, market, promote, or sell any product candidate without obtaining marketing approval from the FDA, the EMA or other comparable regulatory authority, and we may never receive such approvals. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans and will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We may experience numerous unforeseen events prior to, during, or because of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize ETX2514SUL, zoliflodacin, ETX0282CPDP or any of our future product candidates, including:

- the FDA, the EMA or other comparable regulatory authority may change from the views they have expressed to us as to the design or implementation of our clinical trials;

- regulators 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 not reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results; for example, the mortality rate among patients with *Acinetobacter* infections is high and may confound the execution and analysis of our Phase 3 clinical trial;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate, or we may fail to recruit suitable patients to participate in a trial;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators may issue a clinical hold, or regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the FDA, the EMA or other comparable regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with whom we enter into agreements for clinical and commercial supplies;
- 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;
- our product candidates, once exposed to greater numbers of patients, may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the clinical trials; and
- the approval policies or regulations of the FDA, the EMA or other comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

If we are required to conduct additional clinical trials or other testing of ETX2514SUL, zoliflodacin, ETX0282CPDP or any of our future product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials or other testing of ETX2514SUL, zoliflodacin, ETX0282CPDP or any of our future product candidates, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- 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 safety warnings, such as black box warnings or a REMS program;
- be subject to additional post-marketing testing requirements; or
- be required to remove the product from the market after obtaining marketing approval.

Our product development costs may also increase if we experience delays in testing or marketing approvals and we may be required to obtain additional funds to complete clinical trials. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical study or 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. 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 ETX2514SUL, zoliflodacin, ETX0282CPDP or any of our future product candidates.

If we are not successful in discovering, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.

Although a substantial amount of our effort will focus on the continued clinical testing and potential regulatory approval of ETX2514SUL, zoliflodacin and ETX0282CPDP an element of our strategy is to discover, develop and commercialize a portfolio of product candidates to treat serious infections caused by multidrug-resistant Gram-negative bacteria. We are seeking to do so by utilizing our targeted-design platform, which uses bacterial genomics and state-of-the-art molecular and dynamic models to design active new compounds that target validated mechanisms of resistance. We focus our clinical development on multidrug-resistant pathogens and patients with high, unmet medical needs to leverage the development and regulatory paths available for first-in-class or best-in-class antibiotics. Research efforts to identify and develop product candidates require substantial technical, financial and human resources, whether any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable; and
- the FDA, the EMA or other regulatory authorities may not approve or agree with the intended use of a new product candidate.

If we fail to develop and successfully commercialize other current and future product candidates, our business and future prospects may be harmed, and our business will be more vulnerable to any problems that we encounter in developing and commercializing ETX2514SUL, zoliflodacin or ETX0282CPDP.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate, continue or complete clinical trials of ETX2514SUL, zoliflodacin, ETX0282CPDP or any other product candidate that we develop if we and our collaborators are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, the EMA or other comparable regulatory authority. We have limited experience enrolling patients in our clinical trials and cannot predict how successful we will be in enrolling patients in future clinical trials.

For instance, patients involved in our clinical trials are generally in the hospital setting and the decision to participate can be made by the caregiver or doctor. Accordingly, seeking consent for patient participation may become difficult when the family and/or the patient may not be available to consider participation in a clinical trial and the providers/investigators seeking the consent often have no established relationship with the family or patient. This relationship and trust is what many potential participants depend on when making medical decisions, including participating in clinical trials. Patients may also be reluctant to participate in a clinical trial with an investigational drug. In addition, some of our competitors have ongoing clinical trials to treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors. If we are not successful at enrolling patients in one clinical trial, it may affect when we are able to initiate our next clinical trial, which could result in significant delays in our efforts to pursue regulatory approval of and commercialize our product candidates. Patient enrollment is affected by other factors including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity and availability of clinical trial sites for prospective patients;
- the eligibility criteria for participation in the clinical trial;
- the design of the clinical trial;
- the perceived risks and benefits of the product candidate under study;
- our ability to recruit clinical trial investigators with appropriate experience;
- the availability of drugs approved to treat the diseases under study;
- the patient referral practices of physicians;
- our ability to obtain and maintain patient consents;
- the ability to monitor patients adequately during and after treatment; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

Additionally, infections with *Acinetobacter* are relatively uncommon compared to other serious bacterial infections and finding a sufficient number of suitable patients with *Acinetobacter* infections, including patients infected with carbapenem-resistant *Acinetobacter*, to enroll in our planned Phase 3 clinical trial of ETX2514SUL may be a potential challenge. Patients enrolled into the clinical trial may have up to 48-hours of prior antimicrobial therapy to allow for identification of *Acinetobacter* using routine microbiologic culture and organism identification, but this time window may be insufficient in some cases for identifying *Acinetobacter,* thereby limiting patient enrollment. To address this issue, we will be employing a rapid diagnostic for the identification of *Acinetobacter.* We cannot, however, guarantee that each hospital will utilize this rapid diagnostic as part of their screening and enrollment process or if we

will be able to implement the rapid diagnostic in every hospital that is participating in our Phase 3 clinical trial. Additionally, patients with *Acinetobacter* infections are generally very sick and, in some cases, may be unconscious and requiring mechanical ventilation, providing a further potential enrollment challenge. Furthermore, although mortality in some patients is to be expected and is the endpoint of our planned Phase 3 clinical trial of ETX2514SUL, enrollment of near-terminally ill patients could result in a failure to meet our clinical trial endpoints because the patients are too ill to be expected to respond to effective therapy.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would reduce the capital we have available to support our current and future product candidates and may result in our need to raise additional capital earlier than planned and could cause the value of our common stock to decline and limit our ability to obtain additional financing.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their doctor. For example, in the single-ascending dose portion of the Phase 1 clinical trial of ETX0282CPDP, 4 out of 36 subjects experienced mild-to-moderate emesis, or vomiting. We are in the process of analyzing data from these healthy volunteers as well as exploring options to mitigate this effect, including co-administration with food and modified release formulations. Often, it is not possible to determine whether the product candidate being studied caused these conditions. Regulatory authorities may draw different conclusions or require additional testing to confirm these determinations, if they occur. In addition, it is possible that as we test our product candidates in larger, longer and more extensive clinical programs, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. Many times, side effects are only detectable after investigational drugs are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our current product candidates, including ETX2514SUL, zoliflodacin and ETX0282CPDP, or any future product candidates of ours, has side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would harm our business, prospects, operating results and financial condition.

Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed and our ability to generate revenue through their sale may be delayed or eliminated. Any of these occurrences may significantly harm our business, financial condition and prospects.

Additionally, if any of our product candidates receive marketing approval, regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication, or the adoption of a REMS program to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of the drug for distribution to patients and a communication plan to health care practitioners. Furthermore, if we or others later identify undesirable side effects caused by our product candidates, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label or impose distribution or use restrictions;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials, including one or more post-market studies;

- we could be sued and held liable for harm caused to patients;
- we may be required to implement REMS, including the creation of a medication guide outlining the risks of such side effects for distribution to patients;
- we may need to conduct a recall; 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.

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 have a greater likelihood of success.

Because we have limited financial and management resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs 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 products. 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 such product candidate.

We cannot predict whether or when bacteria may develop resistance to our product candidates, which could affect the revenue potential of our product candidates.

We are developing our product candidates to treat drug-resistant bacterial infections. The bacteria responsible for these infections evolve quickly and readily transfer their resistance mechanisms within and between species. Prescription or use of our products, if approved, may depend on the type and rate of resistance of the targeted bacteria. Although we do analyze the potential of our product candidates to develop resistance and only select product candidates that we believe have low resistance potential, we cannot predict whether or when bacterial resistance to our product candidates may develop should our products obtain market approval and be broadly prescribed. The growth of drug-resistant infections in community settings or in countries with poor public health infrastructures, or the potential use of our product candidates outside of controlled hospital settings, could contribute to the rise of resistance. In addition, if resistance in some of our targeted pathogens emerges more slowly than anticipated or fails to emerge in one or more areas where we intend to commercialize our products, we may be unable to enroll patients for certain of our clinical trials and we may fail to obtain regulatory approval for our product candidates, which could affect our ability to generate revenue.

Interim "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim top-line or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

We expect to develop ETX2514 and ETX0282 in combination with approved drugs. If the FDA, the EMA or comparable regulatory authority revokes their approval, we may be unable to obtain approval for our product candidates.

Our lead product candidate, ETX2514, and one of other product candidates, ETX0282, inhibit one of the most prevalent forms of bacterial resistance, β-lactamase enzymes, so-named because of their ability to inactivate β-lactam antibiotics, one of the most commonly used classes of antibiotics. By blocking this resistance mechanism, these product candidates, when administered in combination with β-lactam antibiotics, are designed to restore the efficacy of those antibiotics. ETX2514 is a novel intravenous, or IV, broad-spectrum β-lactamase inhibitor, or BLI, that we are developing in combination with sulbactam, an IV β-lactam antibiotic, for the treatment of a variety of serious multidrug-resistant infections caused by *Acinetobacter*. ETX0282 is a novel, oral BLI that we are developing in combination with cefpodoxime proxetil, or cefpodoxime, an oral β-lactam antibiotic, for the treatment of complicated UTIs, including those caused by extended-spectrum β-lactamase, or ESBL, —producing bacterial strains or carbapenem-resistant *Enterobacteriaceae*, or CRE.

We did not develop or obtain marketing approval for, nor do we manufacture or sell, sulbactam or cefpodoxime or any other currently approved drug that we may study in combination with our product candidates. If the FDA, the EMA or comparable regulatory authority revokes the approval of the drug or drugs in combination with which we determine to develop our product candidates, we may not be able to market our product candidates in such jurisdictions.

Furthermore, if safety or efficacy issues arise with any of these drugs, we could experience significant regulatory delays, and the FDA, the EMA or comparable regulatory authority may require us to redesign or terminate the applicable clinical trials. In addition, if manufacturing or other issues result in a shortage of supply of the drugs with which we determine to combine with our product candidates, we may not be able to complete their clinical development on our current timeline or at all.

Even if our product candidates were to receive marketing approval or be commercialized for use in combination with other existing drugs, we would continue to be subject to the risks that the FDA, the EMA or comparable regulatory authority could revoke approval of the drug used in combination with our product candidates or that safety, efficacy, manufacturing or supply issues could arise with these existing drugs.

Demand for our product candidates, if approved, will depend in part on continued resistance to empirically used broad-spectrum antibiotics and continued use of pathogen identification and resistance profiling in the hospital setting.

Each of our hospital-based product candidates, including ETX2514SUL and ETX0282CPDP, is aimed at treating antibiotic resistant gram-negative bacteria of a specific genus and/or species, such as *Acinetobacter baumannii, Pseudomonas aeruginosa* or certain strains of *Enterobacteriaceae.* Typically, when a patient presents in the hospital with an infection and the bacteria causing the infection is not known or only suspected, a broad-spectrum antibiotic is administered as a first-line empiric treatment pending tests to identify the bacterial pathogen causing the infection and resistance profile. Our product candidates are being developed for use following the identification of the bacterial pathogen and if the resistance profile of the bacterial pathogen suggests that the first-line broad-spectrum antibiotic is not likely to be effective. Our product candidates are designed to treat specific antibiotic-resistant bacteria where broad-spectrum antibiotics are typically not effective due to the development of antibiotic resistance. However, in those cases when first-line treatment with a broad-spectrum antibiotic has been effective, there would not be a need for second-line treatment with our product candidates. If the bacteria we target become less resistant to existing broad-spectrum antibiotics, or if new broad-spectrum antibiotics are developed that are equally effective against the specific bacteria we target, then the potential demand for our product candidates could be diminished.

In addition, while pathogen identification and resistance profiling are common tests that have been employed for decades and are standard practice in hospital microbiology laboratories as a guide for the appropriate use of antibiotics, these tests can be costly and time consuming. If these tests do not remain standard procedure, for example because their coverage and reimbursement status by third-party payors is reduced or eliminated, this could also limit the potential demand for our product candidates.

There are a variety of risks associated with marketing our product candidates internationally, which could affect our business.

We or our collaborators may seek regulatory approval for our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries;
- 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 foreign market with low or lower prices rather than buying them locally;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- various reimbursement, pricing and insurance regimes;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations may compromise our ability to achieve or maintain profitability.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct the clinical trials for our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials or failing to comply with applicable regulatory requirements.

We have engaged contract research organizations, or CROs, to conduct our ongoing and planned clinical trials. We also expect to engage CROs for any of our other product candidates that may progress to clinical development. We expect to rely on CROs, as well as other third parties, such as clinical data management organizations, medical

institutions and clinical investigators, to conduct those clinical trials. Agreements with such third parties might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities would be delayed.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulatory standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Similar regulatory requirements apply outside the United States, including the International Council for Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use, or ICH.

We are also required to register certain ongoing clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so by us or third parties can result in FDA refusal to approve applications based on the clinical data, enforcement actions, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. 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 will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA of any new drug application, or NDA, we submit. Any such delay or rejection could prevent us from commercializing ETX2514SUL, zoliflodacin, ETX0282CPDP or future product candidates.

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

We rely on collaborations with third parties for the development of our product candidates, and we may seek additional collaborations in the future. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We have limited capabilities for drug development and do not yet have any capabilities for sales, marketing or distribution. We are, and expect to continue to be, dependent on collaborations relating to the development and commercialization of our existing and future product candidates. We currently have a collaborative relationship with Zai Lab to develop ETX2514 and ETX2514SUL in the Asia-Pacific region and with GARDP to co-develop zoliflodacin in a Phase 3 clinical trial in uncomplicated gonorrhea. We have had and will continue to have discussions on potential partnering opportunities with various pharmaceutical companies. In addition, we may seek third-party collaborators for the development and commercialization of our product candidates, particularly for the development and commercialization of our product candidates outside the United States. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we fail to enter into or maintain collaborations on reasonable terms or at all, our ability to develop our existing or future product candidates could be delayed, the commercial potential of our products could change, and our costs of development and commercialization could increase. If we enter into any future collaboration arrangements with any third parties, we will likely have limited control over the amount and timing of

resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Our collaborations with Zai Lab, NIAID and GARDP and any future collaborations we might enter into may pose a number of risks, including:

- collaborators often have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected or contractually obligated;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval 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 of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such 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 or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates; and
- collaborators' decisions may limit the availability of the product supplies required for development, clinical and commercial activities.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our drug development or commercialization program could be delayed, diminished or terminated.

The failure of Zai Lab or GARDP to adequately perform their obligations and responsibilities in the conduct of our planned Phase 3 clinical trials of ETX2514SUL and zoliflodacin, respectively, could harm our business because we may not obtain regulatory approval for ETX2514SUL or zoliflodacin in a timely manner, or at all.

We have entered into a license and collaboration agreement with Zai Lab, pursuant to which they will manage the portion of our Phase 3 clinical trial of ETX2514SUL for *Acinetobacter* infections conducted in China. We have also entered into an arrangement with GARDP pursuant to which it is conducting the Phase 3 clinical trial of zoliflodacin in patients with uncomplicated gonorrhea. Under our arrangement with Zai Lab, Zai Lab will fund most of our clinical trial costs in China for ETX2514SUL, including all costs for our planned Phase 3 clinical trial for *Acinetobacter* infections. Under our agreement with GARDP, GARDP will fund all the Phase 3 development costs for zoliflodacin, including costs of the manufacture and supply of the product candidate, and will take the lead in Phase 3 clinical development activities. While we expect to provide operational and logistical support for the planned Phase 3 clinical trials, we have limited control of the activities of our collaborators. We cannot control whether our collaborators will devote sufficient time and resources to the planned Phase 3 clinical trials. If either Zai Lab or GARDP does not successfully carry out its obligations and responsibilities or meet expected deadlines or if the quality or accuracy of the clinical data either obtains is compromised due to the failure to adhere to clinical protocols, regulatory requirements or for other reasons, either of the Phase 3 clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, ETX2514SUL or zoliflodacin. As a result, our results of operations and the commercial prospects for ETX2514SUL or zoliflodacin would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Although Zai Lab and GARDP are each responsible for conducting specified planned Phase 3 clinical trial activities, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on our collaborators does not relieve us of our regulatory responsibilities. We are required to comply with GCP for any product candidate of ours in clinical development. Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we fail to comply with applicable GCP, the clinical data generated in our trials may be deemed unreliable and the FDA or foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, we must conduct our clinical trials with drug product manufactured under current good manufacturing practices, or cGMP, requirements. Failure to comply with any of these regulations may require us to repeat preclinical studies and clinical trials, which would delay the regulatory approval process.

Our reliance on third parties to manufacture our product candidates increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities to produce clinical or commercial supplies of the product candidates that we are developing or evaluating. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We currently rely on third parties for supply of our product candidates, and our strategy is to outsource all manufacturing of our product candidates and approved products, if any, to third parties.

To conduct clinical trials of our product candidates, we will need to identify suitable manufacturers with the capabilities to manufacture our compounds in large quantities in a manner consistent with existing regulations. Our third-party manufacturers may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities and at any other time. If our manufacturers are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed, or infeasible, and regulatory approval or commercial launch of that product candidate may be delayed or not obtained, which could significantly harm our business.

In addition, we plan to develop certain of our product candidates for use as a fixed-dose combination therapy. If manufacturing or other issues result in a supply shortage of sulbactam, cefpodoxime or any other currently approved drug that we may study in combination with ETX2514, ETX0282 or any of our future product candidates, we may not be able to complete clinical development of our product candidates on our current timeline or at all.

We do not currently have any agreements with third-party manufacturers for the long-term commercial supply of any of our product candidates. In the future, we may be unable to enter into agreements with third-party manufacturers for commercial supplies of our product candidates or may be unable to do so on acceptable terms.

Even if we can establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Furthermore, we intend to develop certain product candidates as a fixed-dose combination with β-lactams and only a limited number of cGMP manufacturers are capable of handling β-lactam antibiotics.

If the third parties that we engage to supply any materials or manufacture product for our preclinical tests and clinical trials should cease to continue to do so for any reason, we likely would experience delays in advancing these trials while we identify and qualify replacement suppliers, and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of our product candidates or the substances used to manufacture them or any of approved drug we use in our combination trials, it will be more difficult for us to develop our product candidates and compete effectively.

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

If we are not able to establish collaborations, we may have to alter some of our future development and commercialization plans.

Our product development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the future development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of several factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, the EMA or other comparable regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. Any potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a considerable number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We may not be able to win government or non-profit contracts or grants to fund our product development activities.

Historically, we have relied in part on funding from contracts or grants from government agencies and non-profit entities and it is part of our strategy to continue to do so. Such contracts or grants can be highly attractive because they provide capital to fund the on-going development of our product candidates without diluting our stockholders. However, there is often significant competition for these contracts or grants. Entities offering contracts or grants may have requirements to apply for or to otherwise be eligible to receive certain contracts or grants that our competitors may be able to satisfy that we cannot. In addition, such entities may make arbitrary decisions as to whether to offer contracts or make grants, to whom the contracts or grants will be awarded and the size of the contracts or grants to each awardee. Even if we can satisfy the award requirements, there is no guarantee that we will be selected to receive any contract or grant. If we are not successful in achieving this form of funding for our clinical trials, we will need to seek alternative means of funding which may not be available to the same extent, if at all.

Our reliance on government funding for certain of our programs adds uncertainty to our research, development and commercialization efforts with respect to those programs and may impose requirements that increase the costs of the research, development and commercialization of product candidates developed under those government-funded programs.

Aspects of our development programs are currently being supported, in part, with funding from the NIAID, CARB-X and the U.S. Department of Defense. Contracts and grants awarded by the U.S. government, its agencies and its partners, including our awards from the NIAID, CARB-X and the U.S. Department of Defense, include provisions that reflect the government's substantial rights and remedies, many of which are not typically found in commercial contracts, including powers of the government to:

- terminate agreements, in whole or in part, for any reason or no reason at all;
- provide grant support to potential competitor programs;
- reduce or modify the government's obligations under such agreements without the consent of the other party;

- claim rights, including intellectual property rights, in products and data developed under such agreements;
- audit contract-related costs and fees, including allocated indirect costs;
- suspend the contractor or grantee from receiving new contracts pending resolution of alleged violations of procurement laws or regulations;
- impose U.S. manufacturing requirements for products that embody inventions conceived or first reduced to practice under such agreements;
- suspend or debar the contractor or grantee from doing future business with the government;
- control and potentially prohibit the export of products;
- pursue criminal or civil remedies under the False Claims Act, False Statements Act and similar remedy provisions specific to government agreements; and
- limit the government's financial liability to amounts appropriated by the U.S. Congress on a fiscal-year basis, thereby leaving some uncertainty about the future availability of funding for a program even after it has been funded for an initial period.

We may not have the right to prohibit the U.S. government from using certain technologies developed by us, and we may not be able to prohibit third-party companies, including our competitors, from using those technologies in providing products and services to the U.S. government. The U.S. government generally takes the position that it has the right to royalty-free use of technologies that are developed under U.S. government contracts.

In addition, government contracts and grants, and subcontracts and subawards awarded in the performance of those contracts and grants, normally contain additional requirements that may increase our costs of doing business, reduce our profits, and expose us to liability for failure to comply with these terms and conditions. These requirements include, for example:

- specialized accounting systems unique to government awards;
- mandatory financial audits and potential liability for price adjustments or recoupment of government funds after such funds have been spent;
- adhering to stewardship principals imposed by CARB-X as a condition of the award;
- public disclosures of certain award information, which may enable competitors to gain insights into our research program; and
- mandatory socioeconomic compliance requirements, including labor standards, non-discrimination and affirmative action programs and environmental compliance requirements.

As an organization, we are relatively new to government contracting and new to the regulatory compliance obligations that such contracting entails. If we fail to maintain compliance with those obligations, we may be subject to potential liability and termination of our contracts.

As a U.S. government contractor, we are subject to financial audits and other reviews by the U.S. government of our costs and performance on their contracts, as well as our accounting and general business practices related to these contracts. Based on the results of its audits, the government may adjust our contract-related costs and fees, including allocated indirect costs.

Risks Related to the Commercialization of Our Product Candidates

If we are unable to establish sales, marketing and distribution capabilities for our product candidates, or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing our product candidates, if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product candidate for which we may obtain marketing approval, we will need to establish a sales and marketing organization or enter into collaboration, distribution and other marketing arrangements with one or more third parties to commercialize our product candidates. In the United States, we intend to build a commercial organization to target hospitals with the greatest incidence of serious and life-threatening multidrug-resistant infections and recruit experienced sales, marketing and distribution professionals. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. We plan to work with multi-national pharmaceutical companies to leverage their commercialization capabilities to commercialize any product candidate for which we may obtain regulatory approval outside of the United States.

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 to target the hospital setting 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.

Factors that may inhibit our efforts to commercialize our drugs on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage compared to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- unforeseen costs and limitations regarding setting up a distribution network.

If we are unable to establish our own sales, marketing and distribution capabilities in the United States and, instead, enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to sell, market and distribute any product candidates that we develop ourselves. We intend to use collaborators to assist with the commercialization outside the United States of any of our product candidates that receive regulatory approval. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have limited control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Even if we obtain approvals from the FDA, the EMA or other comparable regulatory agencies and can initiate commercialization of ETX2514SUL, zoliflodacin, ETX0282CPDP or any other product candidates we develop, 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. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the potential and perceived advantages and disadvantages of the product candidates, including cost and clinical benefit relative to alternative treatments;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- acceptance by physicians, patients, operators of hospitals, including in-hospital formularies, 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 ability to manufacture our product in sufficient quantities and yields;
- the strength and effectiveness of marketing and distribution support;
- the prevalence and severity of any side effects;
- 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;
- the emergence of bacterial resistance to the product; and
- the rate at which resistance to other drugs in the target infections grow.

Any failure by any of our product candidates that obtains regulatory approval to achieve market acceptance or commercial success would have a material adverse effect on our business prospects.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition from major multi-national pharmaceutical companies, biotechnology companies, specialty pharmaceutical companies and generic drug companies with respect to ETX2514SUL, zoliflodacin, ETX0282CPDP and other product candidates that we may develop and commercialize in the future. There are several large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of 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, more effectively marketed and sold or less costly than ETX2514SUL, zoliflodacin, ETX0282CPDP or any other product candidates that we may develop, which could render our product candidates non-competitive and obsolete.

We are initially developing ETX2514SUL for the treatment of multidrug-resistant Acinetobacter infections. Due to rising resistance rates, standard-of-care treatment for multidrug-resistant Acinetobacter often includes a combination of several last-line treatment options, including carbapenems, tetracyclines and polymyxins, all generically available agents. We are aware of other potentially competitive approved products, or product candidates in clinical development that have shown in vitro activity against A. baumannii: minocycline, marketed by Melinta Therapeutics Inc., eravacycline, recently approved by the FDA for complicated intra-abdominal infections (CIAI) and TP-6076, currently in a Phase 1 clinical trial, from Tetraphase Pharmaceuticals, Inc. and cefiderocol, currently in a Phase 3 clinical trial, from Shionogi & Co., Ltd.

We are initially developing zoliflodacin for the treatment of gonorrhea. Gonorrhea is commonly treated with the combination therapy of intramuscular ceftriaxone injection and oral azithromycin, both generically available agents. Additional generic cephalosporins and fluoroquinolones are also prescribed, but not recommend as primary treatment options given current resistance rates. Gepotidacin, currently under development for a variety of infections by GlaxoSmithKline plc, is the only potentially competitive product candidate in clinical development that we are aware of that is addressing gonorrhea.

We are initially developing ETX0282CPDP for the treatment of complicated UTIs. There are a variety of generically available antibiotic classes available for the treatment of such infections, including cephalosporins, carbapenems and fluoroquinolones. Additionally, there are several recently approved and likely to be approved branded agents targeting multidrug-resistant complicated UTIs, including Avycaz™, Vabomere™ and Zemdri™. We are aware of additional potentially competitive oral product candidates in clinical development that may address a limited breadth of multidrug-resistant Gram-negative pathogens: sulopenem from Iterum Therapeutics Limited, currently in a Phase 3 clinical trial, C-Scape from Achaogen, Inc., currently in a Phase 1 clinical trial, and tebipenem from Spero Therapeutics Inc., currently in a Phase 1 clinical trial.

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

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 as an organization. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive

than any product candidates that we may develop. Our competitors also may obtain approval from the FDA, the EMA or other comparable regulatory agencies for their product candidates more rapidly than we may obtain approval for ours, which could result in product approval delays if a competitor obtains market exclusivity from the FDA or the EMA, or our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic drugs. Additional drugs may become available on a generic basis over the coming years. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic drugs.

Coverage and adequate reimbursement may not be available for our current or any future product candidates, which could make it difficult for us to sell profitably, if approved.

Market acceptance and sales of any product candidates that we commercialize, if approved, will depend in part on the extent to which reimbursement for these drugs and related treatments will be available from third-party payors, including government health administration authorities, managed care organizations and other private health insurers. Third-party payors decide which therapies they will pay for and establish reimbursement levels. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any product candidates that we develop will be made on a payor-by-payor basis. One payor's determination to provide coverage for a drug does not assure that other payors will also provide coverage and adequate reimbursement for the drug. Additionally, a third-party payor's decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Each payor determines whether it will provide coverage for a therapy, what amount it will pay the manufacturer for the therapy, and on what tier of its list of covered drugs, or formulary, it will be placed. The position on a payor's formulary, generally determines the co-payment that a patient will need to make to obtain the therapy and can strongly influence the adoption of such therapy by patients and physicians. Patients who are prescribed treatments for their conditions and providers prescribing such services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our drugs, and providers are unlikely to prescribe our drugs, unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost of our drugs and their administration.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any drug that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage and reimbursement may impact the demand for, or the price of, any drug for which we obtain marketing approval. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our current and any future product candidates that we develop.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any drugs that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;

- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant costs to defend the resulting litigation;
- substantial monetary awards paid to clinical trial participants or patients;
- loss of revenue; and
- the inability to commercialize any drugs that we may develop.

We currently hold $10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Business and Managing Our Growth

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

We are highly dependent on the management, research and development, clinical, financial and business development expertise of Manoussos Perros, Ph.D., our chief executive officer, Michael Gutch, Ph.D., our chief financial officer and chief business officer, Robin Isaacs, M.D., our chief medical officer, John Mueller, Ph.D., our chief development officer, and Ruben Tommasi, Ph.D., our chief scientific officer, as well as the other members of our scientific and clinical teams. Although we have employment agreements with our executive officers, each of them may nevertheless terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of any of our product candidates, commercialization, manufacturing and sales and marketing personnel, will be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. 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 successfully develop, gain regulatory approval of and commercialize our product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these 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 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 pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of March 15, 2019 we had 33 full-time employees. As the clinical development of our product candidates progresses, we also expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, 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. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Significant disruptions of our information technology systems or data security incidents could result in significant financial, legal, regulatory, business and reputational harm to us.

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, store, process and transmit substantial amounts of sensitive information, including intellectual property, proprietary business information, personal information and other confidential information. It is critical that we do so in a secure manner to maintain the confidentiality, integrity and availability of such sensitive information. We have also outsourced elements of our operations, including elements of our information technology infrastructure, to third parties and, as a result, we manage several third-party vendors who may or could have access to our computer networks or our confidential information. In addition, many of those third parties in turn subcontract or outsource some of their responsibilities to other third parties. While all information technology operations are inherently vulnerable to inadvertent or intentional security breaches, incidents, attacks and exposures, the accessibility and distributed nature of our information technology systems, and the sensitive information stored on those systems, make such systems potentially vulnerable to unintentional or malicious, internal and external attacks on our technology environment. Potential vulnerabilities can be exploited from inadvertent or intentional actions of our employees, third-party vendors, business partners, or by malicious third parties. Attacks of this nature are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives (including industrial espionage) and expertise, including organized criminal groups, “hacktivists,” nation states and others. In addition to the extraction of sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. In addition, the prevalent use of mobile devices increases the risk of data security incidents.

Significant disruptions of our, our third-party vendors’ or business partners’ information technology systems or other similar data security incidents could adversely affect our business operations and result in the loss, misappropriation, and unauthorized access, use or disclosure of, or the prevention of access to, sensitive information, which could result in financial, legal, regulatory, business and reputational harm to us. In addition, information technology system disruptions, whether from attacks on our technology environment or from computer viruses, natural disasters, terrorism, war and telecommunication and electrical failures, could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

There is no way of knowing with certainty whether we have experienced any data security incidents that have not been discovered. While we have no reason to believe this to be the case, attackers have become very sophisticated in the way they conceal access to systems, and many companies that have been attacked are not aware that they have been attacked. Any event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could disrupt our business, harm our reputation, compel us to comply with applicable federal and state breach notification laws and foreign law equivalents, subject us to time-consuming, distracting and expensive litigation, regulatory investigation and oversight, mandatory corrective action, require us to verify the correctness of database contents, or otherwise subject us to liability under laws, regulations and contractual obligations, including those that protect the privacy and security of personal information. This could result in increased costs to us and result in significant legal and financial exposure and reputational harm. In addition, any failure or perceived failure by us or our vendors or business partners to comply with our privacy, confidentiality or data security-related legal or other obligations to third parties, or any further security incidents or other inappropriate access events that result in the unauthorized access, release or transfer of sensitive information, which could include personally

identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation, or public statements against us by advocacy groups or others, and could cause third parties, including clinical sites, regulators or current and potential partners, to lose trust in us, or we could be subject to claims by third parties that we have breached our privacy- or confidentiality-related obligations. Moreover, data security incidents 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. While we have implemented security, measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or security incidents.

If we engage in future acquisitions or strategic collaborations, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

From time to time, we may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary drugs, intellectual property rights, technologies or businesses, as deemed appropriate to carry out our business plan. Any potential acquisition or strategic collaboration may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- assimilation of operations, intellectual property and drugs of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing drug programs and initiatives in pursuing such a strategic partnership, merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing drugs or drug candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or drugs sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and product candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and product candidates may be impaired.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our technology and product candidates. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage that we may have, which could harm our business and ability to achieve profitability. To protect our proprietary positions, we file patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business. The patent application and prosecution process are expensive and time-consuming. We and our current licensees, or any future licensors and licensees may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We or our current licensees, or any future licensors or licensees may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection. Therefore, these and any of our patents and applications

may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If our current licensees, or any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised, and we might not be able to prevent third parties from making, using and selling competing products. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Any of these outcomes could impair our ability to prevent competition from third parties.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Furthermore, recent changes in patent laws in the United States, including the America Invents Act of 2011, may affect the scope, strength and enforceability of our patent rights or the nature of proceedings that may be brought by us related to our patent rights.

We may not be aware of all third-party intellectual property rights potentially relating to our current and future our product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Similarly, should we own any patents or patent applications in the future, we may not be certain that we were the first to file for patent protection for the inventions claimed in such patents or patent applications. As a result, the issuance, scope, validity and commercial value of our patent rights cannot be predicted with any certainty. Moreover, we may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates 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.

Our pending and future patent applications may not result in patents being issued that protect our technology or product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection against competing products or processes sufficient to achieve our business objectives, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may seek to market generic versions of any approved products by submitting abbreviated new drug applications to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable and/or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or

identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

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 our issued patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, trademarks, copyrights or other intellectual property. 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 basis 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. 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 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. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. 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. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. 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 because of the proceedings. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a negative impact on our ability to compete in the marketplace.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could significantly harm our business.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates and use our proprietary chemistry technology without infringing the intellectual property and other proprietary rights of third parties. Numerous third-party U.S. and non-U.S. issued patents exist in the area of antibacterial treatment, including compounds, formulations, treatment methods and synthetic processes that may be applied towards the synthesis of antibiotics. If any of their patents cover our product candidates or technologies, we may not be free to manufacture or market our product candidates as planned.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our technology or product candidates, including interference proceedings before the USPTO. Intellectual property disputes arise in several areas including with respect to patents, use of other proprietary rights and the contractual terms of license arrangements. Third parties may assert claims against us based on

existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative effect on our business.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property rights, including patent rights, that are important or necessary to the development of our product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, and we could be forced to accept unfavorable contractual terms. If we are unable to obtain such licenses on commercially reasonable terms, our business could be harmed.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property 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. Although we try to ensure that our employees do not use the proprietary information or know-how of third parties in their work for us, we may be subject to claims that these employees or we have inadvertently or otherwise used intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. We may also in the future be subject to claims that we have caused an employee to breach the terms of his or her non-competition or non-solicitation agreement. Litigation may be necessary to defend against these potential claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, such employees and contractors may breach the agreement and claim the developed intellectual property as their own.

Our business was founded as a spin-out from AstraZeneca AB, or AstraZeneca. Although all patent applications are fully owned by us and were either filed by AstraZeneca with all rights fully transferred to us, or filed in our sole name, because we acquired certain of our patents from AstraZeneca, we must rely on their prior practices, regarding the assignment of such intellectual property. Our and their assignment agreements may not be self-executing or may be breached, and 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. A court could prohibit us from using technologies or features that are essential to our products if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and could be a distraction to management. In addition, any litigation or threat thereof may adversely affect our ability to hire employees or contract with independent service providers. Moreover, a loss of key personnel or their work product could hamper or prevent our ability to commercialize our products.

Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. Once we select trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose our trademark applications, or otherwise challenge our use of the trademarks. If our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks and we may not have adequate resources to enforce our trademarks.

In addition, any proprietary name we propose to use with ETX2514SUL, zoliflodacin, ETX0282CPDP or any other product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent and trademark protection for our product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any 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 inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. Competitors could purchase our products and replicate some or all the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, 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 competitive position would be harmed.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In some cases, we may not be able to obtain patent protection for certain licensed technology outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we do pursue patent protection 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 pursued and obtained patent protection to develop their own products and, further, may export otherwise 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 preclinical programs 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, if pursued and obtained, or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions 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 our 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.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time-consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize a product candidate.

Our product candidates and the activities associated with their development and commercialization, including their design, research, testing, manufacture, safety, efficacy, quality control, recordkeeping, labeling, packaging, storage, approval, advertising, promotion, sale, distribution, import, export, and reporting of safety and other post-market information, are subject to comprehensive regulation by the FDA, the EMA and other foreign regulatory agencies. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. If any of our product candidates receives marketing approval, the accompanying label may limit its approved use, which could limit sales of the product.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA, the EMA or other regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

In addition, changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause

delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. Any marketing approval we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in these territories. Any approval we are granted for our product candidates in the United States would not assure approval of our product candidates in foreign jurisdictions.

To market and sell our products in the European Union and any other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain approval from the FDA. The regulatory approval process outside the United States generally includes all the risks associated with obtaining approval from the FDA. 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, if at all. 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. However, failure to obtain approval in one jurisdiction may impact our ability to obtain approval elsewhere. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, in June 2016, the electorate in the United Kingdom voted in favor of withdrawing from the European Union, commonly referred to as "Brexit." On March 29, 2017, the United Kingdom formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Treaty on European Union. Since a considerable proportion of the regulatory framework in the United Kingdom is derived from EU directives and regulations, the withdrawal could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, because of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or the European Union for our product candidates, which could significantly and materially harm our business.

Fast Track designation for one or more of our product candidates may not actually lead to a faster development or regulatory review or approval process.

In September 2017, we received Fast Track designation from the FDA for ETX2514SUL for the treatment of a variety of serious multidrug-resistant infections caused by *Acinetobacter*, and in May 2014, we received Fast Track designation for zoliflodacin for the treatment of uncomplicated gonorrhea. If a product is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address the unmet medical need for this condition, a product sponsor may apply for FDA Fast Track designation. Even though we have received Fast Track designation for ETX2514SUL for the treatment of a variety of serious multidrug-resistant infections caused by *Acinetobacter* and for zoliflodacin for the treatment of uncomplicated gonorrhea, Fast Track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with Fast Track designation compared to conventional FDA procedures. In addition, the FDA may withdraw Fast Track designation if it believes that the

designation is no longer supported by data from our clinical development program. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures.

Even if we obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue.

Even if marketing approval of a product candidate is granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation, including the potential requirements to implement a risk evaluation and mitigation strategy or to conduct costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. We must also comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved. In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements including ensuring that quality control and manufacturing procedures conform to cGMP, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMP.

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

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or recall 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 any of them are approved.

The FDA and other federal and state agencies, including the U.S. Department of Justice, or DOJ, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of such requirements may lead to investigations alleging violations of the Food, Drug and Cosmetic Act and other statutes, including the False Claims Act and other federal and state health care fraud and abuse laws as well as state consumer protection laws.

Our failure to comply with all regulatory requirements, and later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;

- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance by us or any future collaborator with regulatory requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with regulatory requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, also can result in significant financial penalties. Similarly, failure to comply with the EU's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

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

We are exposed to the risk of employee fraud or other misconduct or failure to comply with applicable regulatory requirements. Misconduct by employees and independent contractors, such as principal investigators, CROs, consultants, commercial partners and vendors, could include failures to comply with regulations of the FDA, the EMA and other comparable regulatory authorities, to provide accurate information to such regulators, to comply with manufacturing standards we have established, to comply with healthcare fraud and abuse laws, to report financial information or data accurately or to disclose unauthorized activities to us. Sales, marketing and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of business activities, including, but not limited to, research, manufacturing, distribution, pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee and independent contractor misconduct could also involve the improper use of individually identifiable information, including, without limitation, information obtained during clinical trials, which could result in regulatory sanctions and serious harm to our reputation. In addition, federal procurement laws impose substantial penalties for misconduct in connection with government contracts and require certain contractors to maintain a code of business ethics and conduct. It is not always possible to identify and deter employee and independent contractor misconduct, and any precautions we take to detect and prevent improper

activities 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. If any such actions are instituted against us, 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, contractual damages, reputational harm, diminished profits and future earnings, additional reporting or oversight obligations if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with the law and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate.

Our current and future relationships with healthcare professionals, principal investigators, consultants, customers and third-party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, physician payment transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to penalties.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, that may constrain the business or financial arrangements and relationships through which we research, sell, market and distribute any product candidates for which we obtain marketing approval. In addition, we may be subject to physician payment transparency laws and patient privacy and security regulation by the federal government and by the states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws that may affect our ability to operate include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid;

- federal civil and criminal false claims laws, including the federal False Claims Act, which impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the civil monetary penalties statute, which imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal and civil statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose obligations on "covered entities," including certain healthcare providers, health plans, and healthcare clearinghouses, as well as their respective "business associates" that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Physician Payments Sunshine Act, created under Section 6002 of Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, and its implementing regulations, which created annual reporting requirements for manufacturers of drugs, devices, biologicals and medical supplies for certain payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state 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 or to adopt compliance programs as prescribed by state laws and regulations, or that otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and drug pricing; state and local laws requiring the licensure of pharmaceutical sales representatives; and 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 often are not preempted by HIPAA, thus complicating compliance efforts.

Further, the ACA, among other things, amended the intent requirement of the federal Anti-Kickback Statute and certain criminal statutes governing healthcare fraud. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the ACA provided that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Efforts to ensure that our future business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting or oversight obligations if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with the law and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and pursue our strategy. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including future collaborators, are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also affect our business.

Future legislation, and/or regulations and policies adopted by the FDA, the EMA or comparable regulatory authorities, may increase the time and cost required for us or our collaborators to conduct and complete clinical trials of ETX2514SUL, zoliflodacin, ETX0282CPDP and our other product candidates and potential product candidates.

The FDA and the EMA have each established regulations to govern the product development and approval process, as have other foreign regulatory authorities. The policies of the FDA, the EMA and other regulatory authorities

may change. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but not all its provisions have yet been implemented. Additionally, in August 2017, the FDA issued final guidance setting forth its current thinking with respect to development programs and clinical trial designs for antibacterial drugs to treat serious bacterial diseases in patients with an unmet medical need. We cannot predict what if any effect the Cures Act or any existing or future guidance from the FDA or other regulatory authorities will have on the development of our product candidates.

Recently enacted and future legislation may increase the difficulty and cost for us and our collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. For example, the ACA, which was enacted in the United States in March 2010, includes measures to change health care delivery, decrease the number of individuals without insurance, ensure access to certain basic health care services, and contain the rising cost of care. The healthcare reform movement, including the enactment of the ACA, has significantly changed health care financing by both governmental and private insurers in the United States. With respect to pharmaceutical manufacturers, the ACA increased the number of individuals with access to health care coverage, including prescription drug coverage, but it simultaneously imposed, among other things, increased liability for rebates and discounts owed to certain entities and government health care programs, new fees for the manufacture or importation of certain branded drugs, and new transparency reporting requirements under the Physician Payments Sunshine Act.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of any certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or the Tax Act, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, 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." In July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace ACA will impact ACA. We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business. It is uncertain the extent to which any such changes may impact our business or financial condition.

In addition to the ACA, other federal health reform measures have been proposed and adopted in the United States. For example, legislation has been enacted to reduce the level of reimbursement paid to providers under the Medicare program over time, as well as phase in alternative payment models for provider services under the Medicare program with the goal of incentivizing the attainment of pre-defined quality measures. As these measures are not fully in effect, and since the U.S. Congress could intervene to prevent their full implementation, at this time, it is unclear how payment reductions or the introduction of the quality payment program will impact overall physician reimbursement under the Medicare program. It is also unclear if changes in Medicare payments to providers would impact such providers' willingness to prescribe and administer our products, if approved. Further, there has been heightened governmental scrutiny over the way companies set prices for their marketed products. For example, there have been 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 patient programs, and reform government program reimbursement methodologies for drug products.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for drugs. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Our product candidates may be subject to government price controls that may affect our revenue.

There has been heightened governmental scrutiny in the United States and abroad of pharmaceutical pricing practices considering the rising cost of prescription drugs and biologics. In the United States, such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. The Trump administration also released a "Blueprint", or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug 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. On January 31, 2019, the Department of Health and Human Services, Office of Inspector General, proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations. At the state level, legislatures have become 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. Outside of the United States, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

We are subject to the U.K. Bribery Act, the U.S. Foreign Corrupt Practices Act and other anti-corruption laws, as well as export control laws, import and customs laws, trade and economic sanctions laws and other laws governing our operations.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or the Bribery Act, the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. §201, the U.S. Travel Act, and other anti-corruption laws that apply in countries where we do business. The Bribery Act, the FCPA and these other laws generally prohibit us and our employees and intermediaries from authorizing, promising, offering, or providing, directly or indirectly, improper or prohibited payments, or anything else of value, to government officials or other persons to obtain or retain business or gain some other business advantage.

Under the Bribery Act, we may also be liable for failing to prevent a person associated with us from committing a bribery offense. We, our collaborators, and those acting on our behalf operate in a number of jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we participate in collaborations and relationships with third parties whose corrupt or illegal activities could potentially subject us to liability under the Bribery Act, FCPA or local anticorruption laws, even if we do not explicitly authorize or have actual knowledge of such activities. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the way existing laws might be administered or interpreted.

Compliance with the Bribery Act, the FCPA and these other laws is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, anti-corruption laws present 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 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 the United Kingdom, and authorities in the European Union, including applicable export control regulations, economic sanctions and embargoes on certain countries and persons, anti-money laundering laws, import and customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, 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 Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by United States, United Kingdom or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition. Further, the failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological or hazardous materials.

In addition, we may incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Recent and potential future changes to U.S. and non-U.S. tax laws could materially adversely affect our company.

Existing, new or future changes in tax laws, regulations and treaties, or the interpretation thereof, in addition to tax policy initiatives and reforms under consideration in the United States or internationally and other initiatives could have an adverse effect on the taxation of international businesses. Furthermore, countries where we are subject to taxes, including the United States, are independently evaluating their tax policy and we may see significant changes in legislation and regulations concerning taxation. On December 22, 2017, President Trump signed into law new legislation, commonly referred to as the Tax Cuts and Jobs Act, that significantly revises the Code. The Tax Cuts and Jobs Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the Tax Cuts and Jobs Act is uncertain and our business and financial condition could be adversely affected. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. Other legislative changes could also affect the taxation of holders of our common stock. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our effective tax rates in the future in countries where we have operations and have an adverse effect on our overall tax rate in the future, along with increasing the complexity, burden and cost of tax compliance. We urge our stockholders to consult with their legal and tax advisors with respect to any such legislative changes and the potential tax consequences of investing in or holding our common stock.

Risks Related to Ownership of Our Common Stock

The trading price of our common stock may be volatile and fluctuate substantially, and you could lose all or part of your investment.

Since our initial public offering, our stock price has been and is likely to continue to be highly volatile and could be subject to wide fluctuations in response to several factors, some of which are beyond our control, including limited trading volume. The stock market in general and the market for biopharmaceutical companies have experienced extreme volatility that has often been unrelated to the operating performance of companies. As a result of this volatility, investors may not be able to sell their shares at or above the price paid for the shares. In addition to the factors discussed in this "Risk Factors" section, these factors include:

- the commencement, enrollment or results of our planned and future clinical trials;
- the loss of any of our key scientific or management personnel;
- regulatory or legal developments in the United States and other countries;
- the success of competitive products or technologies;

- adverse actions taken by regulatory agencies with respect to our clinical trials or manufacturers;
- changes or developments in laws or regulations applicable to our product candidates and preclinical program;
- changes to our relationships with collaborators, manufacturers or suppliers;
- the results of our testing and clinical trials;
- unanticipated safety concerns;
- announcements concerning our competitors or the pharmaceutical industry in general;
- changes in the structure of healthcare payment systems;
- actual or anticipated fluctuations in our operating results;
- changes in financial estimates or recommendations by securities analysts;
- potential acquisitions;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;
- the trading volume of our common stock on The Nasdaq Global Market;
- sales of our common stock by us, our executive officers and directors or our stockholders or the anticipation that such sales may occur in the future;
- general economic, political, and market conditions and overall fluctuations in the financial markets in the United States or the United Kingdom;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry; and
- investors' general perception of us, our business and the antibiotic sector.

These and other market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their shares of our common stock at or above the price paid for the shares and may otherwise negatively affect the liquidity of our common stock. In addition, the stock market in general, and biopharmaceutical companies, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies.

Some companies that have experienced volatility in the trading price of their shares have been the subject of securities class action litigation. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time-consuming and could divert our management's attention and our resources. Furthermore, during litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our common stock.

An active trading market for our common stock may not continue to develop or be sustained.

Prior to our initial public offering, there was no public market for our common stock. Although our common stock is listed on The Nasdaq Global Market, we cannot assure that an active trading market for our shares will continue to develop or be sustained. If an active market for our common stock does not continue to develop or is not sustained, it may be difficult for investors in our common stock to sell shares without depressing the market price for the shares or to sell the shares at all.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that equity research analysts publish about us and our business. As a newly public company, we have only limited research coverage by equity research analysts. Equity research analysts may elect not to initiate research coverage of our common stock or may discontinue research coverage, and a lack of research coverage may adversely affect the market price of our common stock. We do not have any control over the analysts or the content and opinions included in their reports. The price of our shares could decline if one or more equity research analysts downgrade our shares or issue other unfavorable commentary or research about us. If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our shares could decrease, which in turn could cause the trading price or trading volume of our common stock to decline.

The issuance of additional stock in connection with financings, acquisitions, investments, our equity incentive plan or otherwise will dilute all other stockholders.

Our certificate of incorporation authorizes us to issue up to 125,000,000 shares of common stock and up to 10,000,000 shares of preferred stock with such rights and preferences as may be determined by our board of directors. Subject to compliance with applicable rules and regulations, we may issue our shares of common stock or securities convertible into our common stock from time to time in connection with a financing, acquisition, investment, our equity incentive plans or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and cause the trading price of our common stock to decline.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly. We have outstanding 13,124,842 shares of our common stock as of December 31, 2018. Of these shares, the 5,000,000 shares of our common stock sold in our initial public offering are freely tradable, except shares purchased by our affiliates, and 8,124,842 additional shares of our common stock will be available for sale in the public market beginning in March 2019 following the expiration of lock-up agreements between our stockholders and the underwriters. The representatives of the underwriters may release these stockholders from their lock-up agreements with the underwriters at any time, which would allow for earlier sales of shares in the public market. Moreover, the holders of an aggregate of 8,084,414 shares of our common stock or their transferees will have rights, subject to some conditions, to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If we were to register the resale of these shares, they could be freely sold in the public market. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline. In addition, we intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions and matters submitted to stockholders for approval.

Our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates beneficially own, in the aggregate, 87.3% of our outstanding common stock, based on the number of shares of our common stock outstanding as of December 31, 2018. As a result, these persons, acting together, would be able to control all matters requiring stockholder approval, including the election and removal of directors, any merger, consolidation or sale of all or substantially all our assets, or other significant corporate transactions. The interests of this group of stockholders may not coincide with our interests or the interests of other stockholders. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our common stock by: delaying, deferring, or preventing a change in control; entrenching our management and/or the board of directors; impeding a merger, consolidation, takeover, or other business combination involving us; or by discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

Provisions in our corporate charter documents and under Delaware law could make the acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the way stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a stockholder rights plan, or so-called “poison pill,” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 66 2/3% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting

stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired more than 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, including claims under the Securities Act, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a breach of fiduciary duty;
- any action asserting a claim against us or any of our directors, officers, employees or agents arising under the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws;
- any action or proceeding to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; and
- any action asserting a claim against us or any of our directors, officers, employees or agents that is governed by the internal-affairs doctrine.

Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions.

We are an "emerging growth company" and because of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and

- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We currently take advantage of some or all these reporting exemptions and we may continue to do so until we are no longer an emerging growth company, or EGC. We will remain an EGC until the earlier of (1) the last day of 2023, (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Under Section 107(b) of the JOBS Act, emerging growth companies 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 exemption from new or revised accounting standards and, therefore, we are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, the Sarbanes-Oxley Act and the rules and regulations of The Nasdaq Stock Market, or Nasdaq. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Beginning with our second annual report following our initial public offering, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. Prior to our initial public offering, we have never been required to test our internal controls within a specified period, and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our consolidated financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the Securities and Exchange Commission, or SEC, or other regulatory authorities.

We have broad discretion in the use of our cash and cash equivalents and may invest or spend them in ways with which you do not agree and in ways that may not increase the value of your investment.

Our management will have broad discretion in the application of our cash and cash equivalents and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a negative impact on our business, cause the price of our common stock to decline and delay the development of our product candidates and preclinical program. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. Pursuant to our Business Transfer and Subscription Agreement with AstraZeneca, we also agreed to pay AstraZeneca a one-time milestone payment of $5.0 million within three months of achieving a specified cumulative net sales milestone for ETX2514. This milestone payment will be automatically waived should our common stock trade on Nasdaq at or above a specified price at the time we achieve such specified cumulative net sales milestone for ETX2514, subject to adjustment for share splits, dividends and other similar events. We are also obligated to pay AstraZeneca a one-time milestone payment of $10.0 million within two years of achieving the first commercial sale of zoliflodacin. Following the achievement of either milestone, we are not permitted to pay dividends or make other distributions to any of our stockholders until the applicable milestone payment has been paid in full or otherwise waived. We have never declared or paid a dividend on our common stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, on our common stock will be your sole source of gains for the foreseeable future. Investors seeking cash dividends should not purchase our common stock.

We will incur significantly increased costs because of operating as a company whose common stock is publicly traded in the United States, and our management is required to devote substantial time to new compliance initiatives.

As a public company in the United States, we will incur significant legal, accounting and other expenses that we did not incur previously. These expenses will likely be even more significant after we no longer qualify as an EGC. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq and other applicable securities rules and regulations impose various requirements on public companies in the United States, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our senior management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified senior management personnel or members for our board of directors.

However, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404, we will be required to furnish a report by our senior management on our internal control over financial reporting. However, while we remain an EGC, 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 prepare for compliance with Section 404, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will 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 consolidated financial statements.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our principal offices occupy 20,062 square feet of leased office, research and development and laboratory facility space in Waltham, Massachusetts, pursuant to a lease agreement that expires in December 2022. We believe that our current facilities are suitable and adequate to meet our current needs. We intend to add new facilities or expand existing facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

Item 3. Legal Proceedings

We are not currently a party to any material legal proceedings and we are not aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results or financial condition.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information

Our common stock began trading on The Nasdaq Global Market on September 26, 2018, under the symbol "ETTX." Prior to that time, there was no public market for our common stock.

Holders of Record

As of March 15, 2019, we had approximately 17 holders of record of our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid a dividend on our common stock, and we do not anticipate declaring or paying dividends on our common stock in the foreseeable future. We currently intend to retain our future earnings, if any, to fund the development and growth of our business.

Pursuant to our Business Transfer and Subscription Agreement with AstraZeneca, we agreed to make two specified milestone payments to AstraZeneca. Following the achievement of either milestone, we are not permitted to pay dividends or make other distributions to any of our stockholders until the applicable milestone payment has been paid in full or otherwise waived. See the section titled "Business—Commercial Agreements—Business Transfer and Subscription Agreement with AstraZeneca."

Recent Sales of Unregistered Equity Securities

During the twelve months ended December 31, 2018, we granted to our employees stock options to purchase an aggregate of 243,106 shares of our common stock at an exercise price of $15.00 per share pursuant to our 2018 Equity Incentive Plan and 363,243 shares of our common stock at an exercise price of $6.85 per share pursuant to our Amended and Restated Stock Incentive Plan.

On September 28, 2018, we completed our initial public offering and issued an aggregate of 609,484 shares of our common stock as settlement of the accrued dividends through September 27, 2018 due to the holders of our convertible preferred stock. Holders of our convertible preferred stock were entitled to receive a cumulative preferred dividend at a fixed rate of 4.0% of the issuance price of such preferred stock annually. No dividends will accrue after September 27, 2018.

The offers, sales and issuances of the securities described in this section were exempt from registration either under Rule 701 promulgated under the Securities Act of 1933, as amended, or the Securities Act, in that the transactions were underwritten compensatory benefit plans and contracts relating to compensation, or under Section 4(a)(2) of the Securities Act or Regulation D promulgated under the Securities Act in that the transactions did not involve any public offering within the meaning of Section 4(a)(2) or, in certain cases, were acquired by accredited investors. Appropriate legends were affixed to the securities issued in these transactions.

Use of Proceeds from the IPO

On September 28, 2018, we completed our initial public offering in which we issued and sold 5,000,000 shares of common stock at a price to the public of $15.00 per share, for gross proceeds of $75.0 million and net proceeds of approximately $65.6 million after deducting underwriting discounts and commissions and other offering expenses. None of the expenses associated with the initial public offering were paid to directors, officers, persons owning 10% or more of any class of our equity securities or to their associates, or to our affiliates. The offer and sale of our shares were registered pursuant to a Registration Statement on Form S-1 (Registration No. 333-226920), which was declared effective on September 25, 2018, or the Registration Statement. Credit Suisse Securities (USA) LLC and BMO Capital Markets Corp. acted as lead book-running managers. SunTrust Robinson Humphrey, Inc. and Wedbush Securities Inc. acted as co-managers for the initial public offering. Shares of our common stock began trading on The Nasdaq Global Market on September 26, 2018.

There has been no material change in the planned use of proceeds from our initial public offering as described in our Prospectus that forms a part of our Registration Statement, which was filed with the SEC pursuant to Rule 424 on September 26, 2018. As of December 31, 2018, we consumed approximately $11.6 million of net proceeds from the initial public offering, primarily to advance ETX2514SUL and ETX0282CPDP through clinical trials and manufacture drug supply, and for working capital and general corporate purposes. We invested the remaining funds received in cash equivalents and other marketable securities in accordance with our investment policy.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. Selected Financial Data

As a smaller reporting company, we are not required to provide disclosure for this Item.

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

The following information should be read in conjunction with the consolidated financial information and the notes thereto appearing elsewhere in this Annual Report on Form 10-K.

This discussion contains certain forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Forward-looking statements are identified by words such as "believe," "will," "may," "estimate," "continue," "anticipate," "intend," "should," "plan," "expect," "predict," "could," "potentially" or the negative of these terms or similar expressions. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other "forward- looking" information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in the "Risk Factors" section in this Annual Report on Form 10-K. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. These statements, like all statements in this report, speak only as of their date, and except as required by law, we undertake no obligation to update or revise these statements in light of future developments. We caution investors that our business and financial performance are subject to substantial risks and uncertainties.

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel antibacterial products to treat serious infections caused by multidrug-resistant Gram-negative bacteria. Leveraging our targeted-design platform, we have engineered and developed product candidates that target clinically validated mechanisms to address antibiotic resistance. Our lead product candidate, ETX2514, as well as one of our other product candidates, ETX0282, inhibit one of the most prevalent forms of bacterial resistance, β-lactamase enzymes, so named because of their ability to inactivate β-lactam antibiotics, one of the most commonly used classes of antibiotics. By blocking this resistance mechanism, these product candidates, when administered in combination with β-lactam antibiotics, are designed to restore the efficacy of those antibiotics. Our other product candidate, zoliflodacin, targets the validated mechanism of action of the fluoroquinolone class of antibiotics, but does so in a novel manner to avoid existing fluoroquinolone resistance.

ETX2514SUL is a fixed-dose combination of ETX2514, a novel broad-spectrum intravenous, or IV, β-lactamase inhibitor, or BLI, with sulbactam, an IV β-lactam antibiotic, that we are developing for the treatment of a variety of serious multidrug-resistant infections caused by *Acinetobacter baumannii*, or *Acinetobacter*. We have completed three separate Phase 1 clinical trials, including one evaluating the penetration of ETX2514SUL into the lung and one in renally impaired patients. In addition, we have completed a Phase 2 clinical trial in patients with complicated urinary tract infections, or UTIs. Based on a series of discussions with the U.S. Food and Drug Administration, or FDA, including an end-of-Phase-2 meeting, we are in the process of initiating a single Phase 3 clinical trial with data expected in the second half of 2020.

Zoliflodacin, is a novel orally administered molecule that inhibits bacterial gyrase, an essential enzyme in bacterial reproduction, for the treatment of drug-resistant *Neisseria gonorrhoeae*, the bacterial pathogen responsible for gonorrhea. Intramuscular ceftriaxone now represents the last-resort treatment option for gonorrhea, although resistant strains are beginning to emerge. We believe that there is a growing unmet need for an oral antibiotic that will reliably treat patients with gonorrhea, including multidrug-resistant gonorrhea. We have completed several Phase 1 clinical trials and a Phase 2 clinical trial of zoliflodacin in patients with uncomplicated gonorrhea. The results of the Phase 2 clinical trial were published in the New England Journal of Medicine in November 2018. We intend to initiate a Phase 3 clinical trial in mid-2019 with data expected in 2021. The Phase 3 clinical trial will be funded by our nonprofit collaborator, the Global Antibiotic Research and Development Partnership, or GARDP.

We are also developing ETX0282CPDP for the treatment of complicated UTIs, including those caused by extended-spectrum β-lactamase, or ESBL, producing bacterial strains or carbapenem-resistant *Enterobacteriaceae*, or CRE. ETX0282CPDP is an oral, fixed-dose combination of ETX0282, a novel oral BLI, with cefpodoxime proxetil, an oral β-lactam antibiotic. We believe there is a significant unmet need for new oral antibiotics that reliably treat patients with multidrug-resistant Gram-negative infections. We initiated a multi-part Phase 1 clinical trial of ETX0282CPDP in Australia in the second quarter of 2018 and expect to receive data from the Phase 1 trial in mid-2019.

We are using our targeted-design platform in an attempt to develop a novel class of antibiotics, non β-lactam inhibitors of the penicillin binding proteins, or NBPs. Penicillin binding proteins, or PBPs, are clinically validated targets of β-lactam antibiotics, such as penicillins and carbapenems. Due to their differentiated chemical structure, our NBPs are not subject to inactivation by β-lactamases, unlike β-lactam antibiotics. Accordingly, we believe our NBPs constitute a potential new class of Gram-negative antibacterial agents with no pre-existing resistance that are designed to target a broad spectrum of pathogens, including *Pseudomonas aeruginosa,* or *Pseudomonas*. We expect to select an initial clinical candidate from our NBP program in 2019.

Since our inception in May 2015, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, acquiring or discovering product candidates and securing related intellectual property rights, conducting discovery and development activities for our programs and planning for potential commercialization. We do not have any products approved for sale and have not generated any revenue from product sales. As of December 31, 2018, we have funded our operations primarily with net cash proceeds of $104.2 million from the sale of our preferred stock and net cash proceeds of approximately $65.6 million from the sale of common stock in our initial public offering. We have also either directly received funding or financial commitments from, or have had our program activities conducted and funded by, the U.S. government through our arrangements with the U.S. National Institute of Allergy and Infectious Diseases, or NIAID, the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program, or CARB-X, and the U.S. Department of Defense, and have received non-profit awards from GARDP, and an upfront payment from our license and collaboration agreement with Zai Lab (Shanghai), Co., Ltd., or Zai Lab.

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 one or more of our current or future product candidates and programs. Our net loss was $33.0 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of $90.1 million. We anticipate that a substantial portion of our capital resources and efforts in the foreseeable future will be focused on completing the necessary development, obtaining regulatory approval and preparing for potential commercialization of our product candidates.

We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. Our net losses may fluctuate significantly from period to period, depending on the timing of our planned clinical trials and expenditures on other research and development activities. We expect our expenses will increase substantially over time as we:

- continue our ongoing and planned preclinical and clinical development of our product candidates;
- initiate preclinical studies and clinical trials for any additional product candidates that we may pursue in the future;
- seek to discover and develop additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any product candidate for which we may obtain regulatory approval and intend to commercialize on our own;

- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, scientific and chemistry, manufacturing and controls personnel; and
- add additional operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

Furthermore, we now incur additional costs associated with operating as a public company that we did not previously incur or previously incurred at lower rates, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

Initial Public Offering; Reverse Stock Split

On September 28, 2018, we completed our initial public offering, in which we issued and sold 5,000,000 shares of common stock at a price to the public of $15.00 per share. The aggregate net proceeds to us from the initial public offering were approximately $65.6 million after deducting underwriting discounts and commissions and offering expenses payable by us. The shares began trading on The Nasdaq Global Market on September 26, 2018. Upon the completion of the initial public offering, all of our outstanding shares of redeemable convertible preferred stock, including accrued dividends, automatically converted into 8,084,414 shares of our common stock. In September 2018, we also effected a 1-for-20.728 reverse stock split of our issued and outstanding common stock. All of our historical share and per share information shown in the accompanying consolidated financial statements and related notes have been retroactively adjusted to give effect to the reverse stock split.

The Corporate Reorganization

We completed a corporate reorganization on April 23, 2018. As part of the corporate reorganization, we formed Entasis Therapeutics Holdings Inc., a Delaware corporation, in March 2018 with nominal assets and liabilities for the purpose of consummating the corporate reorganization described herein. In connection with the corporate reorganization, the existing shareholders of Entasis Therapeutics Limited exchanged their shares for the same number and classes of newly issued shares in Entasis Therapeutics Holdings Inc. As a result, Entasis Therapeutics Limited became a wholly owned subsidiary of Entasis Therapeutics Holdings Inc.

Upon completion of the corporate reorganization on April 23, 2018, the historical consolidated financial statements of Entasis Therapeutics Limited became the historical consolidated financial statements of Entasis Therapeutics Holdings Inc.

Funding Arrangements

In December 2016, we entered into a funding arrangement with the U.S. Army Medical Research Acquisition Activity, or USAMRAA, a division of the U.S. Department of Defense, through which we received a grant. This grant covers funding for up to $1.1 million of specified research expenditures incurred from December 2016 through June 2019, or the performance period. Specified research expenditures are the reimbursable expenses associated with agreed upon activities needed to advance the research project supported by the grant. These expenditures can include internal labor, laboratory supplies and equipment, travel, consulting and third-party vendor research and development support costs. We have until September 30, 2022 to obtain reimbursements from USAMRAA for the fully paid, specified research expenditures incurred during the performance period. As of December 31, 2018, we had received $0.9 million of funding and we had recorded $1.0 million of grant income under this grant.

In March 2017 and October 2017, we entered into funding arrangements with the Trustees of Boston University to utilize funds from the U.S. government, through the CARB-X program, for support of the ETX0282 and NBP programs. These funding arrangements will cover up to $16.4 million of our specified research expenditures from April 2017 through September 2021. As of December 31, 2018, we had received $4.5 million in funding and we had recorded $5.7 million of grant income under this grant.

In July 2017, we entered into a collaboration agreement with GARDP for the development and commercialization of a product candidate containing zoliflodacin in certain countries. Under the terms of the collaboration agreement, GARDP will fully fund the Phase 3 clinical trial, including the manufacture and supply of the product candidate containing zoliflodacin, in uncomplicated gonorrhea.

In April 2018, we entered into a license and collaboration agreement with Zai Lab (Shanghai) Co., Ltd., or Zai Lab, pursuant to which Zai Lab licensed exclusive rights to ETX2514 and ETX2514SUL in the Asia-Pacific region. Under the terms of the agreement, Zai Lab will fund most of our clinical trial costs in China for ETX2514SUL, including all costs in China for our planned Phase 3 clinical trial of ETX2514SUL, with the exception of patient drug supply. As of December 31, 2018, we had received payments of $4.5 million, the $5.0 million upfront payment and $0.3 million of research support payments, less applicable taxes, from Zai Lab and we had recognized revenue of $5.0 million under the agreement.

Components of Results of Operations

Revenue

All of our revenue has been derived from our license and collaboration agreement with Zai Lab. To date, we have not generated any revenue from product sales, and we do not expect to generate any revenue from the sale of products in the near future. If our development efforts for our product candidates and preclinical program are successful and result in regulatory approval, we may generate revenue in the future from product sales.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our product discovery efforts and the development of our preclinical and clinical product candidates. These expenses include:

- employee-related expenses, including salaries and benefits, travel and stock-based compensation expense for employees engaged in research and development functions;
- fees paid to consultants for services directly related to our product development and regulatory efforts;
- expenses incurred under agreements with contract research organizations, or CROs, as well as contract manufacturing organizations, or CMOs, and consultants that conduct and provide supplies for our preclinical studies and clinical trials;
- costs associated with preclinical activities and development activities;
- costs associated with our technology and our intellectual property portfolio;
- costs related to compliance with regulatory requirements; and
- facilities-related expenses, which include allocated rent and maintenance of facilities and other operating costs.

Costs associated with research and development activities are expensed as incurred. Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or other information provided to us by our vendors. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are

delivered or the related services are performed, or until it is no longer expected that the goods will be delivered, or the services rendered.

Our direct research and development expenses are tracked on a program-by-program basis for our product candidates and preclinical program and consist primarily of external costs, such as fees paid to outside consultants, CROs, CMOs and central laboratories in connection with our preclinical development, process development, manufacturing and clinical development activities. Our direct research and development expenses by program also include fees incurred under service, license or option agreements. We do not allocate employee costs or facility expenses to specific programs because these costs are deployed across multiple programs and, accordingly, are not separately classified. We primarily use internal resources and our own employees to conduct our research and discovery as well as for managing our preclinical development, process development, manufacturing and clinical development activities.

To date, substantially all of our research and development expenses have been related to the preclinical and clinical development of our product candidates and preclinical program. The following table shows our research and development expenses by development program and type of activity for the years ended December 31, 2018 and 2017:

	Year Ended December 31,		
	2018	2017	$ Change
	(in thousands)		
Direct research and development expenses by program:			
ETX2514	$ 15,745	$ 11,137	$ 4,608
ETX0282	4,593	5,303	(710)
Zoliflodacin	73	71	2
Other preclinical programs	2,610	1,247	1,363
Unallocated expenses:			
Personnel related (including stock-based compensation)	7,091	5,865	1,226
Facility related and other	2,934	2,122	812
Total research and development expenses	$ 33,046	$ 25,745	$ 7,301

Research and development activities are central to our business model. Product candidates in later 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. We expect our research and development expenses to increase over the next several years as we progress our product candidates through clinical development. However, it is difficult to determine with certainty the duration and completion costs of our current or future preclinical programs and clinical trials of our product candidates, or if, when or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates.

The duration, costs and timing of clinical trials and development of our product candidates and preclinical program will depend on a variety of factors that include, but are not limited to, the following:

- the number of trials required for approval and any requirement for extension trials;
- per-patient trial costs;
- the number of patients that participate in the trials;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;

- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up; and
- the efficacy and safety profiles of the product candidates.

Any changes in the outcome of any of these factors with respect to the development of our product candidates could mean a significant change in the costs and timing associated with the development of these product candidates. In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing and supply, and commercial viability. We will determine which programs to pursue and how much to fund each program based on the scientific and clinical success of each product candidate, as well as an assessment of each candidate's commercial potential.

General and Administrative Expenses

General and administrative expenses consist of salaries and benefits, travel and stock-based compensation expense for personnel in executive, finance and administrative functions. General and administrative costs also include facilities-related costs not otherwise included in research and development expenses, professional fees for legal, patent, consulting and accounting and audit services.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will continue to incur increased accounting, audit, legal, regulatory, compliance and 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 a regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and other employee-related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing functions for that product candidate.

Other Income

Grant Income

Grant income consists of income recognized in connection with grants we received under our funding arrangements with USAMRAA and the Trustees of Boston University through the CARB-X program. Grant income is recognized in the period during which the related specified expenses are incurred, provided that the conditions under which the grants were provided have been met.

Interest Income

Interest income consists of interest earned on our cash and investment balances. Our interest income has not been significant due to low interest earned on invested balances.

Income Taxes

Income taxes consist of China withholding taxes on the upfront payment under our license and collaboration agreement with Zai Lab.

Results of Operations

Years Ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017:

	Year Ended December 31,		
	2018	2017	$ Change
	(in thousands)		
Revenue	$ 5,000	$ —	$ 5,000
Operating expenses:			
Research and development	33,046	25,745	7,301
General and administrative	10,161	5,599	4,562
Total operating expenses	43,207	31,344	11,863
Loss from operations	(38,207)	(31,344)	(6,863)
Other income:			
Grant income	5,337	1,396	3,941
Interest income	390	25	365
Total other income	5,727	1,421	4,306
Loss before income taxes	(32,480)	(29,923)	(2,557)
Provision for income taxes	472	—	472
Net loss	$ (32,952)	$ (29,923)	$ (3,029)

Revenue

We recognized revenue of $5.0 million for the year ended December 31, 2018 compared to zero for the prior year. The revenue in 2018 was attributable to executing the exclusive license and completing the initial technology transfer of licensed know-how pursuant to the collaboration agreement with Zai Lab, which we entered into in April 2018.

Research and Development Expenses

Research and development expenses were $33.0 million for the year ended December 31, 2018, compared to $25.7 million for the year ended December 31, 2017. The increase of $7.3 million was primarily due to an increase of $6.0 million in preclinical and clinical development expenses related to the advancement of ETX2514SUL and our NBP and other preclinical programs, an increase of $1.2 million in personnel expenses associated with higher headcount and higher stock-based compensation primarily related to 2017 and 2018 option grants, and an increase of $0.8 million associated with higher facility costs and an increase in loss on disposal of fixed assets, offset in part by a decrease of $0.7 million in preclinical and clinical development expenses associated with our ETX0282CPDP product candidate. The increase in preclinical and clinical development expenses of $6.0 million was associated with the advancement of ETX2514SUL and our NBP and other preclinical programs and was primarily due to an increase of $3.0 million in clinical development costs, an increase of $2.3 million in drug manufacturing costs and an increase of $0.7 million in preclinical expenses.

General and Administrative Expenses

General and administrative expenses were $10.2 million for the year ended December 31, 2018, compared to $5.6 million for the year ended December 31, 2017. The increase of $4.6 million was primarily due to increases of $2.5 million in legal and professional fees associated with our initial public offering and preparation for becoming a public company and the preparation, audit and review of our consolidated financial statements, $0.6 million in salaries and benefits resulting from higher headcount, $0.5 million in stock-based compensation expense resulting from options granted during the years ended December 31, 2017 and December 31, 2018, $0.3 million in value-added taxes associated with payments received from Zai Lab and $0.7 million in other costs, such as facilities and insurance.

Other Income

Other income was $5.7 million for the year ended December 31, 2018, compared to $1.4 million for the year ended December 31, 2017. The increase of $4.3 million was due to an increase in grant income of $3.9 million associated with our grant agreements with the CARB-X program and an increase in interest income of $0.4 million resulting from higher cash balances during the year ended December 31, 2018.

Income Taxes

Income taxes consists of China withholding taxes on the upfront payment under our license and collaboration agreement with Zai Lab.

Liquidity and Capital Resources

Overview

As of December 31, 2018, we had raised aggregate net cash proceeds of $104.2 million from the sale of redeemable convertible preferred stock and approximately $65.6 million of net proceeds from the sale of common stock in our initial public offering, which we have used to fund our operations. In addition, we have also either directly received funding or financial commitments from, or have had our program activities conducted and funded by, the U.S. government through our arrangements with NIAID, CARB-X and the U.S. Department of Defense, and have received non-profit awards from GARDP and an upfront payment from Zai Lab. As of December 31, 2018, we had cash, cash equivalents and short-term investments of $85.1 million.

We have incurred operating losses and experienced negative operating cash flows since our inception and anticipate that we will continue to incur losses for at least the next several years. Our net loss was $33.0 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of $90.1 million.

We believe that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2020. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research and development services, laboratory and related supplies, manufacturing development costs, legal and other regulatory expenses and general administrative costs.

The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the clinical development of our product candidates and obtain regulatory approvals. We are also unable to predict when, if ever, net cash inflows will commence from product sales. This is due to the numerous risks and uncertainties associated with developing drugs, including, among others, the uncertainty of:

- successful enrollment in, and completion of clinical trials;
- performing preclinical studies and clinical trials in compliance with the FDA, the EMA or any comparable regulatory authority requirements;
- the ability of collaborators to manufacture sufficient quantity of product for development, clinical trials or potential commercialization;

- obtaining marketing approvals with labeling for sufficiently broad patient populations and indications, without unduly restrictive distribution limitations or safety warnings, such as black box warnings or a Risk Evaluation and Mitigation Strategies program;
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third parties for manufacturing capabilities;
- launching commercial sales of products, if and when approved, whether alone or in collaboration with others;
- acceptance of the therapies, if and when approved, by physicians, patients and third-party payors;
- competing effectively with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- protecting our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of our drugs following approval.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that product candidate.

We will not generate revenue from product sales unless and until we or a collaborator successfully complete clinical development and obtain regulatory approval for our current and future product candidates. If we obtain regulatory approval for any of our product candidates that we intend to commercialize on our own, we will incur significant expenses related to commercialization, including developing our internal commercialization capability to support product sales, marketing and distribution.

As a result, we will need substantial additional funding to support our continuing operations and to pursue our growth strategy. Until such time, if ever, when we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaboration, license and development agreements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. 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.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to 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 drug development or future commercialization efforts or grant rights to a third party to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our failure to raise capital as and when needed would compromise our ability to pursue our business strategy.

We will also continue to incur costs as a public company that we did not previously incur or previously incurred at lower rates, including increased fees payable to the nonemployee members of our board of directors, increased personnel costs, increased director and officer insurance premiums, audit and legal fees, investor relations fees and expenses for compliance with public-company reporting requirements under the Exchange Act and rules implemented by the SEC and Nasdaq.

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, we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

Cash Flows

The following table summarizes our cash flows for the periods presented (in thousands):

	Year Ended December 31,	
	2018	2017
Net cash used in operating activities	$ (35,817)	$ (27,159)
Net cash used in investing activities	(36,091)	(286)
Net cash provided by financing activities	66,167	56,290
Net (decrease) increase in cash and cash equivalents	$ (5,741)	$ 28,845

Operating Activities

During the year ended December 31, 2018, operating activities used $35.8 million of cash, resulting from our net loss of $33.0 million and net cash used for changes in operating assets and liabilities of $4.5 million, partially offset by non-cash charges of $1.6 million. Net cash used for changes in operating assets and liabilities for the year ended December 31, 2018 consisted primarily of a $2.3 million decrease in accrued expenses and other current liabilities, a $1.5 million increase in prepaid expenses and other assets and a $1.0 million increase in grants receivable. These were partially offset by a $0.1 million increase in accounts payable and a $0.1 million increase in deferred rent.

During the year ended December 31, 2017, operating activities used $27.2 million of cash, resulting from our net loss of $29.9 million, partially offset by non-cash charges of $0.6 million and net cash provided by changes in operating assets and liabilities of $2.2 million. Net cash provided by changes in operating assets and liabilities for the year ended December 31, 2017 consisted primarily of a $3.4 million increase in accrued expenses and a $0.4 million increase in accounts payable, mainly due to an increase in clinical trial costs and associated drug manufacturing costs for the advancement of ETX2514 and ETX0282. These increases were partially offset by an increase of $0.7 million in grants receivable, an increase of $0.3 million in prepaid expenses and a decrease of $0.6 million in due to related party.

Investing Activities

During the year ended December 31, 2018, net cash used in investing activities was $36.1 million, consisting of our purchases of property and equipment of $0.4 million and short-term investments of $35.7 million.

During the year ended December 31, 2017, net cash used in investing activities was $0.3 million, consisting of our purchases of property and equipment.

Financing Activities

During the year ended December 31, 2018, net cash provided by financing activities was $66.2 million, which consisted primarily of $66.1 million of proceeds from our initial public offering net of issuance costs paid in the period.

During the year ended December 31, 2017, net cash provided by financing activities was $56.3 million, which related to sales of redeemable convertible preferred stock. In August 2017, we issued and sold 42,372,882 shares of Series B-1 Tranche A redeemable convertible preferred stock for net proceeds of $24.4 million and in December 2017, we received net cash proceeds of $31.9 million from the sale of 54,067,796 shares of Series B-1 Tranche B redeemable convertible preferred stock.

Contractual Obligations and Commitments

As a smaller reporting company, we are not required to provide the disclosure required by Item 303(a)(5) of Regulation S-K.

Off-Balance Sheet Arrangements

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

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, costs and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing at the end of this 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.

Revenue Recognition

Effective January 1, 2018, we adopted Accounting Standards Codification, or ASC, Topic 606, Revenue from Contracts with Customers, or ASC 606. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, and financial instruments. Under ASC 606, we recognize revenue when a customer obtains control of promised goods or services, in an amount that reflects the consideration that we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations, and assesses whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied as services are rendered.

We enter into collaboration agreements for research, development, manufacturing and commercial services that are within the scope of ASC 606, under which we license certain rights to our product candidates to third parties. The terms of these arrangements typically include payment to us of one or more of the following: non-refundable, upfront license fees; reimbursement of certain costs; customer option exercise fees; development, regulatory and commercial milestone payments; and royalties on net sales of licensed products. The amount of variable consideration is constrained until it is probable that the revenue is not at a significant risk of reversal in a future period. The contracts into which we enter generally do not include significant financing components.

As part of the accounting for these arrangements, we may be required to use significant judgment to determine: (a) the performance obligations in the contract under step (ii) above, (b) the transaction price under step (iii) above and (c) the timing of revenue recognition, including the appropriate measure of progress in step (v) above. We use judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the

transaction price, as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. If a milestone or other variable consideration relates specifically to our efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, we generally allocate the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur.

Amounts received prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date would be classified as current portion of deferred revenue in our consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date would be classified as deferred revenue, net of current portion.

Licenses of intellectual property

In assessing whether a license is distinct from the other promises, we consider factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can benefit from a license for its intended purpose without the receipt of the remaining promise(s), whether the value of the license is dependent on the unsatisfied promise(s), whether there are other vendors that could provide the remaining promise(s), and whether it is separately identifiable from the remaining promise(s). For licenses that are combined with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Customer options

If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. We evaluate the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent or include a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. We allocate the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised.

Milestone payments

At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. We evaluate factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant reversal of cumulative revenue would not occur. At the end of each subsequent reporting period, we reevaluate the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and earnings in the period of adjustment.

Research and Development Expenses

All research and development expenses are expensed as incurred. Research and development expenses comprise costs incurred in performing research and development activities, including compensation, benefits and other

employee costs; equity-based compensation expense; laboratory and clinical supplies and other direct expenses; facilities expenses; overhead expenses; fees for contractual services, including preclinical studies, clinical trials, clinical manufacturing and raw materials; and other external expenses. Nonrefundable advance payments for research and development activities are capitalized and expensed over the related service period or as goods are received. When third-party service providers' billing terms do not coincide with our period-end, we are required to make estimates of our obligations to those third parties, including clinical trial costs, contractual service costs and costs for supply of our drug candidates, incurred in a given accounting period and record accruals at the end of the period. We base our estimates on our knowledge of the research and development programs, services performed for the period and the expected duration of the third-party service contract, where applicable.

Stock-Based Compensation

We measure stock-based awards granted to employees and directors based on the estimated fair value of the award on the date of the grant and recognize compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. Forfeitures are accounted for as they occur.

We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model. We consider the fair value of our common stock, an input to the Black-Scholes option pricing model, a critical accounting estimate.

Valuation of Common Stock

As there was no public market for our common stock prior to the initial public offering of our common stock, the estimated fair value of our common stock was determined by our board of directors as of the date of each option grant, with input from management, considering third-party valuations of our common stock 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. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*.

Our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- any recent valuations of our common stock performed by an independent third-party valuation firm;
- our financial position, including cash-on-hand, and our historical and forecasted performance and operating results;
- the status of research and development efforts;
- our stage of development and business strategy;
- the material risks related to our business;
- the prices at which we sold our redeemable convertible preferred stock to outside investors in arm's length transactions and the rights, preferences and privileges of the redeemable convertible preferred stock relative to those of our common stock, including the liquidation preferences of the redeemable convertible preferred stock;
- the illiquid nature of our common stock;
- the value of companies we consider peers based on a number of factors, including similarity to us with respect to industry, business model, stage of growth, company size, financial risk and other factors;

- trends and market conditions affecting our industry; and
- the likelihood of achieving a liquidity event for the holders of our common stock, such as an initial public offering or the sale of our company.

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 stock-based compensation expense could be materially different.

Following the closing of the initial public offering, the fair value of our common stock is determined based on the quoted market price of our common stock.

Recent Accounting Pronouncements

Refer to Note 2, "Summary of Significant Accounting Policies," in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a discussion of recent accounting pronouncements.

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.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

As a smaller reporting company, we are not required to provide disclosure for this Item.

Item 8. Financial Statements and Supplementary Data

Our financial statements, together with the report of our independent registered public accounting firm, appear in this Annual Report on Form 10-K beginning on page F-1.

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

We maintain "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, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's, or SEC's, rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, 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.

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2018. Based on the evaluation of our disclosure controls and procedures as of December 31, 2018, 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

Due to a transition period established by SEC rules applicable to newly public companies, our management is not required to evaluate the effectiveness of our internal control over financial reporting until after the filing of our Annual Report on Form 10-K for the year ended December 31, 2018.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption for "emerging growth companies."

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting that occurred during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers, and Corporate Governance

The information required by this item is incorporated by reference to the information set forth in the sections titled "Proposal 1 – Election of Directors," "Executive Officers," and "Information Regarding the Board and Corporate Governance" and "Section 16(a) Beneficial Ownership Reporting Compliance" in our 2019 Proxy Statement.

Item 11. Executive Compensation

The information required by this item is incorporated by reference to the information set forth in the section titled "Executive Officer and Director Compensation" in our 2019 Proxy Statement.

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

The information required by this item is incorporated by reference to the information set forth in the section titled "Security Ownership of Certain Beneficial Owners and Management and "Equity Compensation Plan Information" in our 2019 Proxy Statement.

Item 13. Certain Relationships and Related Transactions and Director Independence

The information required by this item is incorporated by reference to the information set forth in the section titled "Transactions with Related Persons" and "Information regarding the Board and Corporate Governance – Board Independence" in our 2019 Proxy Statement.

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference to the information set forth in the section titled "Independent Registered Public Accounting Firm Fees" contained in Proposal 2 in our 2019 Proxy Statement.

PART IV

Item 15. Exhibits, Financial Statements and Schedules

(a)(1) Financial Statements.

The response to this portion of Item 15 is set forth under Item 8 hereof.

(a)(2) Financial Statement Schedules.

All schedules have been omitted because they are not required or because the required information is given in the Financial Statements or Notes thereto.

(a)(3) Exhibits.

The exhibits listed below are filed as part of this Form 10-K other than Exhibit 32.1, which shall be deemed furnished

Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Company (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on September 28, 2018).
3.2	Amended and Restated Bylaws of the Company (incorporated herein by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 001-38670), filed with the SEC on September 28, 2018).
4.1	Form of Common Stock Certificate of the Company (incorporated herein by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
4.2	Registration Rights Agreement, by and among the Company and certain of its stockholders, dated September 14, 2018 (incorporated herein by reference to Exhibit 4.2 to the Company's Registration Statement on Form S-1/A (File No. 333-226920), filed with the SEC on September 18, 2018).
10.1+	Form of Indemnification Agreement by and between the Company and each of its directors and officers (incorporated herein by reference to Exhibit 10.16 to the Company's Registration Statement on Form S-1/A (File No. 333-226920), filed with the SEC on September 18, 2018).
10.2+	2018 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (File No. 001-38670), filed with the SEC on November 14, 2018).
10.3+	Forms of Stock Option Grant Notice and Stock Option Agreement under the 2018 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).

10.4+	Forms of Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under the 2018 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.5+	2018 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q (File No. 001-38670), filed with the SEC on November 14, 2018).
10.6+	Amended and Restated Stock Incentive Plan (incorporated herein by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.7+	Form of Nonqualified Stock Option Agreement (Senior Management) under the Amended and Restated Stock Incentive Plan (incorporated herein by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.8+	Form of Incentive Stock Option Agreement (Senior Management) under the Amended and Restated Stock Incentive Plan (incorporated herein by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.9+	Employment Agreement between the Company and Manoussos Perros, effective September 25, 2018 (incorporated herein by reference to Exhibit 10.13 to the Company's Registration Statement on Form S-1/A (File No. 333-226920), filed with the SEC on September 18, 2018).
10.10+	Employment Agreement between the Company and Michael Gutch, effective September 25, 2018 (incorporated herein by reference to Exhibit 10.14 to the Company's Registration Statement on Form S-1/A (File No. 333-226920), filed with the SEC on September 18, 2018).
10.11+	Employment Agreement between the Company and Robin Isaacs, effective September 25, 2018 (incorporated herein by reference to Exhibit 10.15 to the Company's Registration Statement on Form S-1/A (File No. 333-226920), filed with the SEC on September 18, 2018).
10.12+	Employment Agreement between the Company and Ruben Tommasi, effective September 25, 2018
10.13†	Amended and Restated Business Transfer and Subscription Agreement, dated as of March 29, 2016, by and among AstraZeneca AB, AstraZeneca UK Limited, AstraZeneca Pharmaceuticals LP, and the Company (incorporated herein by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.14†	Amendment to Amended and Restated Business Transfer and Subscription Agreement, dated as of August 28, 2017, by and among AstraZeneca AB, AstraZeneca UK Limited, AstraZeneca Pharmaceuticals LP, and the Company (incorporated herein by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.15†	Amendment No. 2 to Amended and Restated Business Transfer and Subscription Agreement, dated as of January 30, 2018, by and among AstraZeneca AB, AstraZeneca UK Limited, AstraZeneca Pharmaceuticals LP, and the Company (incorporated herein by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).

10.16†	Collaboration Agreement, dated as of July 4, 2017, by and between the Drugs for Neglected Diseases initiative, acting through the Global Antibiotic Research and Development Partnership, and the Company (incorporated herein by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
10.17	Novation of Contract, dated January 11, 2019, by and between the Global Antibiotic Research and Development Partnership and the Company.
10.18†	License and Collaboration Agreement, dated April 25, 2018, by and between Zai Lab (Shanghai) Co., Ltd. and the Company (incorporated herein by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (File No. 333-226920), filed with the SEC on August 17, 2018).
21.1	Subsidiaries of Entasis Therapeutics Holdings Inc.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on the signature page to this report).
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.
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.
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Furnished herewith and not deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

\+ Indicates a management contract or compensatory plan.

† Confidential treatment has been granted with respect to portions of this exhibit (indicated by asterisks) and those portions have been separately filed with the Securities and Exchange Commission.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

ENTASIS THERAPEUTICS HOLDINGS INC.

Date: March 29, 2019

By: /s/ Manoussos Perros
Manoussos Perros, Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Manoussos Perros, Ph.D. and Michael Gutch, Ph.D., and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue thereof.

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

Signature	Title	Date
/s/ Manoussos Perros Manoussos Perros, Ph.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 29, 2019
/s/ Michael Gutch Michael Gutch, Ph.D.	Chief Business Officer and Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 29, 2019
/s/ Nicholas Galaktos Nicholas Galakatos, Ph.D.	Director	March 29, 2019
/s/ Heather Behanna Heather Behanna, Ph.D.	Director	March 29, 2019
/s/ David C. Hastings David C. Hastings	Director	March 29, 2019
/s/ Gregory Norden Gregory Norden	Director	March 29, 2019
/s/ Heather Preston Heather Preston, M.D.	Director	March 29, 2019
/s/ Andrew J. Staples Andrew J. Staples	Director	March 29, 2019
/s/ James Topper James Topper, M.D., Ph.D.	Director	March 29, 2019

ENTASIS THERAPEUTICS HOLDINGS INC.
Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Entasis Therapeutics Holdings Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Entasis Therapeutics Holdings Inc. and subsidiaries (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for the years then ended, 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, 2018 and 2017, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2017.

Cambridge, Massachusetts
March 29, 2019

ENTASIS THERAPEUTICS HOLDINGS INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 49,360	$ 55,101
Short-term investments	35,732	—
Grants receivable	1,706	722
Prepaid expenses and other current assets	1,994	497
Total current assets	88,792	56,320
Property and equipment, net	419	646
Deferred offering costs	—	1,765
Other assets	63	63
Total assets	$ 89,274	$ 58,794
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 1,370	$ 2,218
Accrued expenses and other current liabilities	4,846	7,615
Total current liabilities	6,216	9,833
Deferred rent	175	38
Total liabilities	6,391	9,871
Commitments (Note 14)		
Series A redeemable convertible preferred stock, par value $0.001; 0 and 33,499,900 shares authorized, issued and outstanding as of December 31, 2018 and 2017	—	23,866
Series B redeemable convertible preferred stock, par value $0.001; 0 and 25,000,000 shares authorized, issued and outstanding as of December 31, 2018 and 2017	—	24,550
Series B-1 Tranche A redeemable convertible preferred stock, par value $0.001; 0 and 42,372,882 shares authorized, issued and outstanding as of December 31, 2018 and 2017	—	24,423
Series B-1 Tranche B redeemable convertible preferred stock, par value $0.001; 0 and 54,067,796 shares authorized, issued and outstanding as of December 31, 2018 and 2017	—	31,874
Stockholders' equity (deficit):		
Common stock, par value $0.001; 125,000,000 shares authorized and 13,124,842 shares issued and outstanding as of December 31, 2018; 250,000,000 shares authorized; 12,639 shares issued and outstanding as of December 31, 2017	13	3
Additional paid-in capital	172,988	1,377
Accumulated other comprehensive loss	(9)	—
Accumulated deficit	(90,109)	(57,170)
Total stockholders' equity (deficit)	82,883	(55,790)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 89,274	$ 58,794

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

ENTASIS THERAPEUTICS HOLDINGS INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share data)

	Year Ended December 31,	
	2018	2017
Revenue	$ 5,000	$ —
Operating expenses:		
Research and development	33,046	25,745
General and administrative	10,161	5,599
Total operating expenses	43,207	31,344
Loss from operations	(38,207)	(31,344)
Other income:		
Grant income	5,337	1,396
Interest income	390	25
Total other income	5,727	1,421
Loss before income taxes	(32,480)	(29,923)
Provision for income taxes	472	—
Net loss	(32,952)	(29,923)
Dividends declared	(9,142)	—
Net loss attributable to common stockholders—basic and diluted	$ (42,094)	$ (29,923)
Net loss per share attributable to common stockholders—basic and diluted	$ (12.31)	$ (13,795.76)
Weighted average common stock outstanding—basic and diluted	3,419,720	2,169

	Year Ended December 31,	
	2018	2017
Other comprehensive loss		
Net loss	$ (32,952)	$ (29,923)
Net unrealized loss on investments held	(9)	—
Comprehensive loss	$ (32,961)	$ (29,923)

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

ENTASIS THERAPEUTICS HOLDINGS INC.
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share data)

	Redeemable Convertible Preferred Stock								Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	A		B		B-1 A		B-1 B							
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balances as of December 31, 2016	33,499,900	$ 23,866	25,000,000	$ 24,550	—	$ —	—	$ —	4	$ —	$ 904	$ —	$ (27,247)	$ (26,343)
Issuance of series B-1	—	—	—	—	42,372,882	24,423	54,067,796	31,874	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	420	—	—	420
Exercise of stock options	—	—	—	—	—	—	—	—	12,635	3	53	—	—	56
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(29,923)	(29,923)
Balances as of December 31, 2017	33,499,900	23,866	25,000,000	24,550	42,372,882	24,423	54,067,796	31,874	12,639	3	1,377	—	(57,170)	(55,790)
ASU 2018-07 modified retrospective adjustment	—	—	—	—	—	—	—	—	—	—	(13)	—	13	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	1,201	—	—	1,201
Reorganization adjustment	—	—	—	—	—	—	—	—	—	(3)	3	—	—	—
Conversion of preferred stock into common stock upon initial public offering	(33,499,900)	(23,866)	(25,000,000)	(24,550)	(42,372,882)	(24,423)	(54,067,796)	(31,874)	8,084,414	8	104,705	—	—	104,713
Issuance of common stock upon initial public offering, net of issuance costs of $9,378	—	—	—	—	—	—	—	—	5,000,000	5	65,619	—	—	65,624
Exercise of stock options	—	—	—	—	—	—	—	—	27,789	—	96	—	—	96
Unrealized loss on investments held	—	—	—	—	—	—	—	—	—	—	—	(9)	—	(9)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(32,952)	(32,952)
Balances as of December 31, 2018	—	$ —	—	$ —	—	$ —	—	$ —	13,124,842	$ 13	$ 172,988	$ (9)	$ (90,109)	$ 82,883

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

ENTASIS THERAPEUTICS HOLDINGS INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2018	2017
Cash flows from operating activities:		
Net loss	$ (32,952)	$ (29,923)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	164	194
Stock-based compensation expense	1,201	420
Loss on disposal of property and equipment	282	—
Amortization and accretion of investments	(21)	—
Changes in operating assets and liabilities:		
Grants receivable	(984)	(722)
Prepaid expenses and other assets	(1,497)	(345)
Accounts payable	133	447
Due to related party	—	(620)
Accrued expenses and other current liabilities	(2,280)	3,386
Deferred rent	137	4
Net cash used in operating activities	(35,817)	(27,159)
Cash flows from investing activities:		
Purchases of property and equipment	(370)	(286)
Purchases of short-term investments	(35,721)	—
Net cash used in investing activities	(36,091)	(286)
Cash flows from financing activities:		
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	56,531
Proceeds from exercise of stock options	96	56
Proceeds from initial public offering, net of issuance costs paid during the year	66,071	(297)
Net cash provided by financing activities	66,167	56,290
Net (decrease) increase in cash and cash equivalents	(5,741)	28,845
Cash and cash equivalents at beginning of the year	55,101	26,256
Cash and cash equivalents at end of the year	$ 49,360	$ 55,101
Supplemental disclosure of non-cash investing and financing activities:		
Purchases of property and equipment included in accounts payable	$ 37	$ 190
Initial public offering costs included in accounts payable and accrued expenses	$ 150	$ —
Deferred offering costs included in accounts payable and accrued expenses	$ —	$ 1,468
Conversion of preferred stock to common stock upon initial public offering	$ 104,713	$ —
Supplemental disclosure of cash flow information:		
Cash paid for taxes	$ 472	$ —

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

ENTASIS THERAPEUTICS HOLDINGS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Description of Business

Entasis Therapeutics Holdings Inc. ("Entasis" or the "Company") is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel antibacterial products to treat serious infections caused by multidrug-resistant Gram-negative bacteria. The Company has three subsidiaries: Entasis Therapeutics Limited; Entasis Therapeutics Inc.; and Entasis Therapeutics Security Corporation.

The Company was initially formed as Entasis Therapeutics Limited ("Entasis Limited") on March 6, 2015 in the United Kingdom ("U.K.") as a wholly owned subsidiary of AstraZeneca AB ("AstraZeneca"). In connection with the spin-out of Entasis Limited from AstraZeneca in May 2015, Entasis Limited issued 4 ordinary shares to AstraZeneca. Additionally, pursuant to a business transfer and subscription agreement with AstraZeneca (the "A Subscription Agreement"), Entasis Limited also issued 33,499,900 shares of A redeemable convertible preference shares ("A Preferred Stock") to AstraZeneca in May 2015. In March 2016, Entasis Limited issued 25,000,000 shares of B redeemable convertible preference shares ("B Preferred Stock") to third-party investors, at which point AstraZeneca no longer held a controlling interest in Entasis Limited.

On April 23, 2018, Entasis Limited completed a corporate reorganization (the "Reorganization"). As part of the Reorganization, Entasis Limited formed Entasis Therapeutics Holdings Inc., a Delaware corporation, in March 2018 with nominal assets and liabilities for the purpose of consummating the Reorganization. In connection with the Reorganization, the existing shareholders of Entasis Limited exchanged each of their classes of shares of Entasis Limited for the same number and classes of common stock and preferred stock of Entasis Therapeutics Holdings Inc. on a one-to-one basis. The newly issued stock of Entasis Therapeutics Holdings Inc. have substantially identical rights to the exchanged shares of Entasis Limited. As a result of the exchange, Entasis Therapeutics Holdings Inc. became the sole shareholder of Entasis Limited. Upon the completion of the Reorganization on April 23, 2018, the historical consolidated financial statements of Entasis Limited became the historical consolidated financial statements of Entasis Therapeutics Holdings Inc.

On September 28, 2018, the Company completed an initial public offering of its common stock, in which the Company issued and sold 5,000,000 shares of common stock at a price to the public of $15.00 per share. The aggregate net proceeds to the Company from the initial public offering were approximately $65.6 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company. Upon the completion of the Company's initial public offering, all of the outstanding shares of redeemable convertible preferred stock of the Company, including accrued dividends, automatically converted into 8,084,414 shares of the Company's common stock.

Risks and Uncertainties

As of December 31, 2018, the Company had $85.1 million in cash, cash equivalents and short-term investments and an accumulated deficit of $90.1 million. Since its inception through December 31, 2018, the Company has funded its operations primarily with proceeds from the sale of redeemable convertible preferred stock and the sale of its common stock. The Company has also either directly received funding or financial commitments from, or has had its program activities conducted and funded by, United States ("U.S.") government agencies and non-profit entities. In the absence of positive cash flows from operations, the Company is highly dependent on its ability to find additional sources of funding in the form of debt or equity financing. The Company believes its existing cash, cash equivalents and short-term investments will enable it to fund its operating expenses and capital requirements into the fourth quarter of 2020.

As an early-stage company, the Company is subject to a number of risks common to other life science companies, including, but not limited to, raising additional capital, development by its competitors of new technological innovations, risk of failure in preclinical and clinical studies, safety and efficacy of its product candidates in clinical trials, the risk of relying on external parties such as contract research organizations ("CROs") and contract manufacturing organizations ("CMOs"), the regulatory approval process, market acceptance of the Company's products

once approved, lack of marketing and sales history, dependence on key personnel and protection of proprietary technology. The Company's therapeutic programs are currently pre-commercial, spanning discovery through early development and will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization of any product candidates. These efforts require significant amounts of additional capital, adequate personnel, infrastructure, and extensive compliance-reporting capabilities. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate revenue from product sales. The Company may never achieve profitability, and unless and until it does, it will continue to need to raise additional capital or obtain financing from other sources, such as strategic collaborations or partnerships.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). The consolidated financial statements include the accounts of Entasis Therapeutics Holdings Inc. and its wholly owned subsidiaries: Entasis Therapeutics Limited; Entasis Therapeutics Inc.; and Entasis Therapeutics Security Corporation. All intercompany accounts and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with U.S. GAAP requires management to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expenses during the reporting period. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the recognition of revenue, the recognition of research and development expenses and the valuation of common stock used in the determination of stock-based compensation expense. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ from the Company's estimates.

Fair Value Measurements

The accounting standard for fair value measurements defines fair value, establishes a framework for measuring fair value in accordance with U.S. GAAP, and requires detailed disclosures about fair value measurements. Under this standard, fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The valuation techniques are based on observable and unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, while unobservable inputs reflect the Company's assumptions. This standard classifies these inputs into the following hierarchy:

Level 1 Inputs— Quoted prices in active markets for identical instruments;

Level 2 Inputs—Quoted prices for similar instruments in active markets; quoted prices for identical or similar instruments in markets that are not active; and model-derived valuations whose inputs are observable or whose significant value drivers are observable;

Level 3 Inputs—Instruments with primarily unobservable value drivers.

The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between Level 1, Level 2 or Level 3 during the years ended December 31, 2018 and 2017.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include cash held in banks, money market instruments, corporate and municipal notes, U.S. Treasury securities and federal agency securities. Cash equivalents are stated at fair value. The amount of cash equivalents included in cash and cash equivalents was approximately $38.6 million and zero at December 31, 2018 and 2017, respectively.

Short-term Investments

The Company classifies all short-term investments with an original maturity when purchased of greater than three months as available-for-sale. Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported in other comprehensive loss. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Realized gains and losses, and declines in value judged to be other than temporary on available-for-sale securities, are included in interest income.

The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest income. To determine whether an other-than-temporary impairment exists, the Company considers whether it has the ability and intent to hold the investment until a market price recovery, and whether evidence indicating the recoverability of the cost of the investment outweighs evidence to the contrary.

Concentrations of Credit Risk and of Significant Suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and short-term investments. Periodically, the Company maintains deposits in accredited financial institutions in excess of federally insured limits. The Company maintains each of its cash balances with high-quality, accredited, financial institutions and, accordingly, such funds are not exposed to significant credit risk. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party manufacturers to supply drug substance products for research and development activities for its programs, including preclinical testing. These programs could be adversely affected by a significant interruption in the supply of such drug substance products.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' equity (deficit) as a reduction of proceeds generated as a result of the offering.

Should a planned equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the consolidated statement of operations. The Company recorded deferred offering costs of $1.8 million as of December 31, 2017.

Property and Equipment

Property and equipment is recorded at cost and depreciated over the estimated useful lives of the related assets using the straight-line method. Upon disposal of an asset, the related cost and accumulated depreciation are removed from the asset accounts and any resulting gain or loss is included in the consolidated statement of operations. Repair and maintenance costs are expensed as incurred, whereas major improvements are capitalized as additions to property and equipment. The estimated useful lives of the Company's respective assets are as follows:

	Estimated Useful Life
Laboratory equipment	3 - 5 years
Computer software	3 years
Computer equipment	3 years
Furniture and fixtures	5 years

Impairment of Long-Lived Assets

Long-lived assets are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Whenever such events occur, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows.

Segment Information

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. As of December 31, 2018 and 2017, all of the Company's long-lived assets were domiciled in the United States.

Revenue Recognition

Effective January 1, 2018, the Company adopted Accounting Standards Codification, or ASC, Topic 606, Revenue from Contracts with Customers, or ASC 606. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, and financial instruments. Under ASC 606, the Company recognizes revenue when a customer obtains control of promised goods or services, in an amount that reflects the consideration that the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assessed the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied as services are rendered.

The Company enters into collaboration agreements for research, development, manufacturing and commercial services that are within the scope of ASC 606, under which the Company licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, upfront license fees; reimbursement of certain costs; customer option exercise fees; development, regulatory and commercial milestone payments; and royalties on net sales of licensed products. The

amount of variable consideration is constrained until it is probable that the revenue is not at a significant risk of reversal in a future period. The contracts into which the Company enters generally do not include significant financing components.

As part of the accounting for these arrangements, the Company may be required to use significant judgment to determine: (a) the performance obligations in the contract under step (ii) above, (b) the transaction price under step (iii) above and (c) the timing of revenue recognition, including the appropriate measure of progress in step (v) above. The Company uses judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price, as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. If a milestone or other variable consideration relates specifically to the Company's efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, the Company generally allocates the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur.

Amounts received prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date would be classified as current portion of deferred revenue in the consolidated balance sheet. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date would be classified as deferred revenue, net of current portion.

Licenses of intellectual property

In assessing whether a license is distinct from the other promises, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from a license for its intended purpose without the receipt of the remaining promise(s), whether the value of the license is dependent on the unsatisfied promise(s), whether there are other vendors that could provide the remaining promise(s), and whether it is separately identifiable from the remaining promise(s). For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Customer options

If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent or include a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised.

Milestone payments

At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control, such as regulatory approvals, are not considered probable of being achieved until those

approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant reversal of cumulative revenue would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and earnings in the period of adjustment.

See Note 8 for a further discussion of accounting for revenue.

Government Contracts and Grant Agreements

Income from grants is recognized in the period during which the related specified expenses are incurred, provided that the conditions under which the grants or incentives were provided have been met. Grant funding that is received by the Company in advance of incurring specified expenses is recorded in the consolidated balance sheet as a liability. Grant income recognized upon incurring specified expenses in advance of receipt of grant funding is recorded in the consolidated balance sheet as a receivable.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses include employee costs, such as salaries, equity-based compensation and benefits, as well as consulting, contract research, third-party license fees, depreciation, rent and other corporate or operational costs attributable to the Company's research and development activities. These costs include allocated facility-related expenses and external costs of outside vendors engaged to conduct both preclinical studies and clinical trials. Non-refundable pre-payments for goods or services that will be used or rendered for future research and development activities are deferred. Such amounts are recognized as expense as the goods or services are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

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. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

The Company expenses patent costs as incurred and records such costs within general and administrative expenses.

Stock-Based Compensation

The Company measures stock-based awards granted based on the estimated fair value of the award on the date of the grant and recognizes compensation expense for those awarded to employees and directors over the requisite service period, which is generally the vesting period of the respective award, and for those awarded to nonemployees over the period during which services are rendered by nonemployees until completed. Forfeitures are accounted for as they occur. The Company has issued stock-based awards with only service-based vesting conditions and records the expense for these awards using the straight-line method. The Company has not issued any stock-based awards with performance-based vesting conditions.

The Company adopted ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07") in 2018. *Refer to Recently Adopted Accounting Pronouncements* below for further information. The standard expands the scope of ASC 718 to include all share-based payment arrangements related to the acquisition of goods and services from both nonemployees and employees. Prior to the adoption of ASU 2018-07, for equity awards granted to nonemployees, the Company accounted for the related equity award compensation in accordance with the provisions of ASC 718 and ASC Topic 505, *Equity*, and recognized equity award compensation expense over the related service period of the nonemployee award. Equity awards issued to nonemployees were recorded at their fair values, using the then-current fair value of the incentive units, common stock and updated assumption inputs in the Black-Scholes option-pricing model, as applicable, and were periodically revalued as the equity instruments vested. After the adoption of ASU 2018-07, equity-classified share-based payment awards issued to nonemployees are measured at grant date fair value similarly to those of employees and are no longer revalued as the equity instruments vest. The new standard allows entities to use the expected term to measure nonemployee options or elect to use the contractual term as the expected term, on an award-by-award basis.

The Company classifies stock-based compensation expense in its consolidated statement of operations in the same manner in which the award recipients' payroll costs are classified or in which the award recipients' service payments are classified.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option pricing model. As there was no public market for the Company's common stock prior to the initial public offering of its common stock, the estimated fair value of common stock was determined by the Company's board of directors as of the date of each option grant, with input from management, considering third party valuations of its common stock as well as the Company's 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. These third party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately Held Company Equity Securities Issued as Compensation*. The Company also lacked company-specific historical and implied volatility information for its stock. Therefore, the Company estimates its expected stock price volatility based on the historical volatility of publicly traded peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method. The "simplified" method estimates the expected term of stock options as the mid-point between the weighted average time to vesting and the contractual maturity. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. There is no expected dividend yield since the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future.

Income Taxes

The Company accounts for income taxes using the asset and liability method which requires for the recognition of deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the carrying amounts and the tax bases of assets and liabilities. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. A valuation allowance is provided to reduce the deferred tax asset to a level which, more likely than not, will be realized. See Note 12 for further discussion of income taxes.

Accounting for income taxes requires a two-step approach to recognize and measure uncertain tax positions. The first step is to evaluate the tax position for recognition by determining if, based on the technical merits, it is more likely than not that the position will be sustained upon audit, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount that is more than 50 percent likely of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Net Loss Per Share

Basic and diluted net loss per share is determined by dividing net loss by the weighted-average common stock outstanding during the period. For all periods presented, outstanding stock options, A Preferred Stock, B Preferred Stock, Series B-1 A redeemable convertible preferred stock ("B-1 A Preferred Stock") and Series B-1 B redeemable convertible preferred stock ("B-1 B Stock") have been excluded from the calculation because their effects would be anti-dilutive. Therefore, the weighted-average shares used to calculate both basic and diluted loss per share are the same.

Recently Adopted Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standard Update ("ASU") No. 2014-09, *Revenue from Contracts with Customers (Topic 606)* ("ASU 2014-09"), which supersedes existing revenue recognition guidance under GAAP. The standard's core principle is that a company will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those goods or services. The standard defines a five-step process to achieve this principle, and will require companies to use more judgment and make more estimates than under the current guidance. ASU 2014-09 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, and is effective for public entities for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. In March 2016, the FASB issued ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations* ("ASU 2016-08"), which further clarifies the implementation guidance on principal versus agent considerations in ASU 2014-09. In April 2016, the FASB issued ASU No. 2016-10, *Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing*, clarifying the implementation guidance on identifying performance obligations and licensing. Specifically, the amendments in this update reduce the cost and complexity of identifying promised goods or services and improve the guidance for determining whether promises are separately identifiable. The amendments in this update also provide implementation guidance on determining whether an entity's promise to grant a license provides a customer with either a right to use the entity's intellectual property (which is satisfied at a point in time) or a right to access the entity's intellectual property (which is satisfied over time). The Company adopted this guidance in connection with the execution of the license and collaboration agreement (the "Zai Agreement") with Zai Lab (Shanghai) Co., Ltd. ("Zai Lab") in April 2018. Prior to the Zai Agreement, the Company did not have any revenue from contracts with customers.

In October 2016, the FASB issued ASU No. 2016-16, *Income Taxes (Topic 740): Intra-Entity Transfer of Assets Other than Inventory* ("ASU 2016-16"), which requires the recognition of the income tax consequences of an intra-entity transfer of an asset, other than inventory, when the transfer occurs. The standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. On January 1, 2018, the Company adopted this guidance, and the adoption did not have a material impact on the Company's consolidated financial statements and related disclosures.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230), Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"). The amendments of ASU 2016-15 were issued to address eight specific cash flow issues for which stakeholders have indicated to the FASB that a diversity in practice existed in how entities were presenting and classifying these items in the statement of cash flows. The issues addressed by ASU 2016-15 include but are not limited to the classification of debt prepayment and debt extinguishment costs, payments made for contingent consideration for a business combination, proceeds from the settlement of insurance proceeds, distributions received from equity method investees and separately identifiable cash flows and the application of the predominance principle. The amendments of ASU 2016-15 are effective for public entities for fiscal years beginning after December 15, 2017 and interim periods in those fiscal years. The adoption of ASU 2016-15 is required to be applied retrospectively. On January 1, 2018, the Company adopted this guidance and the adoption did not have a material impact on the Company's consolidated financial statements and related disclosures.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"), which clarifies when to account for a change to the terms or conditions of a

share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. The standard is effective for annual periods beginning after December 15, 2017. On January 1, 2018, the Company adopted this guidance and the adoption did not have a material impact on the Company's consolidated financial statements and related disclosures.

In June 2018, the FASB issued ASU 2018-07, which expands the scope of Topic 718 to include share-based payment awards to nonemployees. The amendments in ASU 2018-07 are effective for public business entities for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. For all other entities, the amendments are effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. During the year ended December 31, 2018, the Company early adopted this guidance and the adoption did not have a material impact on the Company's consolidated financial statements and related disclosures.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU 2016-02 – *Leases (Topic 842)*, which replaces the existing accounting guidance for leases. This standard requires entities that lease assets to recognize the assets and liabilities for the rights and obligations created by those leases on the balance sheet. The standard is effective for fiscal years and the interim periods within those fiscal years beginning after December 15, 2018. The guidance is required to be applied by the modified retrospective transition approach and early adoption is permitted. In July 2018, the FASB issued ASU 2018-11 Leases – Targeted Improvements, intended to ease the implementation of the new lease standard for financial statement preparers by, among other things, allowing for an additional transition method. In lieu of presenting transition requirements to comparative periods, as previously required, an entity may now elect to show a cumulative effect adjustment on the date of adoption without the requirement to recast prior period financial statements or disclosures presented in accordance with ASU 2016-02. The Company expects to adopt the new standard and elect to use the cumulative effect adjustment transition option effective January 1, 2019, which will be the initial date of application per ASU 2018-11.

The Company expects to elect the available package of practical expedients which allows it to not reassess previous accounting conclusions around whether arrangements are or contain leases, the classification of its leases, and the treatment of initial direct costs. The Company also expects it will make an accounting policy election to keep leases with an initial term of 12 months or less off of the balance sheet. The Company is continuing to evaluate developments within the new lease guidance and is finalizing its evaluation of its existing population of contracts to ensure all contracts that meet the definition of a lease contract under the new standard are identified. The Company has assessed the impact that the adoption of this guidance will have on its financial statements and footnote disclosures. The standard will have a material impact on the consolidated balance sheet related to the recognition of right-of-use assets and lease liabilities for operating leases. The standard will not have a material impact on the consolidated statement of operations.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement,* which eliminates, adds and modifies certain disclosure requirements for fair value measurements. The guidance is effective for all entities for fiscal years beginning after December 15, 2019 and for interim periods within those fiscal years, but entities are permitted to early adopt either the entire standard or only the provisions that eliminate or modify the requirements. The Company does not expect the adoption of the new guidance to have a material effect on its consolidated financial statements.

In November 2018, the FASB issued ASU No. 2018-18 — *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606.* This update clarifies the interaction between Topic 808, Collaborative Arrangements, and Topic 606, Revenue from Contracts with Customers. The standard is effective for fiscal years and the interim periods within those fiscal years beginning after December 15, 2019. The guidance is required to be applied retrospectively to the date of initial application of Topic 606. An entity should recognize the cumulative effect of initially applying the amendments as an adjustment to the opening balance of retained earnings of the later of the earliest annual period presented and the annual period that includes the date of the entity's initial

application of Topic 606. The Company is currently assessing the impact that adoption of this guidance will have on its consolidated financial statements.

3. Short-term Investments

The following table summarizes the amortized cost and estimated fair value of the Company's marketable securities, which are considered to be available-for-sale investments and were included in short-term investments on the consolidated balance sheets:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(in thousands)			
Balance at December 31, 2018:				
U.S. government-sponsored enterprise securities	$ 6,059	$ —	$ —	$ 6,059
U.S. Treasury securities	29,680	—	(7)	29,673
Total	$ 35,739	$ —	$ (7)	$ 35,732

Certain short-term debt securities with original maturities of less than 90 days are included in cash and cash equivalents on the consolidated balance sheets and are not included in the tables above. At December 31, 2018, all investments have contractual maturities within one year. The Company had no investments at December 31, 2017.

4. Fair Value of Financial Instruments

The following tables set forth the Company's assets that were accounted for at fair value on a recurring basis as of December 31, 2018:

	December 31, 2018			
	Fair Value Measurement Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Cash equivalents:				
Money market funds	$ 18,609	$ —	$ —	$ 18,609
U.S. Treasury securities	19,964	—	—	19,964
Short-term investments:				
U.S. government-sponsored enterprise securities	—	6,059	—	6,059
U.S. Treasury securities	29,673	—	—	29,673
Total	$ 68,246	$ 6,059	$ —	$ 74,305

The Company classifies its money market funds and U.S. Treasury securities as Level 1 assets under the fair value hierarchy as these assets have been valued using quoted market prices in active markets without any valuation adjustment. The Company classifies its corporate and municipal notes as Level 2 assets under the fair value hierarchy, as these assets have been valued using information obtained through a third-party pricing service at each balance sheet date, using observable market inputs that may include trade information, broker or dealer quotes, bids, offers, or a combination of these data sources.

The carrying amounts of the Company's cash equivalents, grants receivable, accounts payable and accrued expenses approximate their fair value due to the short-term nature of these amounts.

5. Property and Equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2018	2017
Laboratory equipment	$ 929	$ 1,036
Computer software	71	71
Computer equipment	38	7
Furniture and fixtures	6	—
Total	1,044	1,114
Less: accumulated depreciation	(625)	(468)
Property and equipment, net	$ 419	$ 646

Depreciation expense was $0.2 million for each of the years ended December 31, 2018 and 2017.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2018	2017
Accrued compensation and benefits	$ 1,526	$ 1,286
Accrued contract manufacturing	1,003	3,633
Accrued clinical costs	752	1,096
Accrued professional services	672	1,246
Accrued research costs	364	135
Other	529	219
Total accrued expenses and other current liabilities	$ 4,846	$ 7,615

7. Funding Arrangements

In December 2016, the Company entered into a funding arrangement with the U.S. Army Medical Research Acquisition Activity (the "USAMRAA grant") that covers up to $1.1 million of specified research expenditures of the Company incurred from December 2016 through June 2019 (the "performance period"). The Company has until September 2022 to obtain the reimbursements from USAMRAA for the specified research expenditures incurred and paid by the Company during the performance period.

The Company recognized grant income of $0.5 million and $0.5 million for the years ended December 31, 2018 and 2017, respectively. The Company received $0.9 million of funding under the grant for the year ended December 31, 2018 and no funding under the grant for the year ended December 31, 2017. The Company recorded a receivable to reflect unreimbursed, eligible costs incurred under the grant in the amount of $0.2 million and $0.5 million as of December 31, 2018 and December 31, 2017, respectively.

In March 2017 and October 2017, the Company entered into funding arrangements with the Trustees of Boston University to utilize funds from the U.S. government through the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator ("CARB-X") program. These funding arrangements will cover up to $16.4 million of specified research expenditures of the Company from April 2017 through September 2021.

The Company recognized grant income in connection with the CARB-X agreements of $4.8 million and $0.9 million for the years ended December 31, 2018 and 2017, respectively. The Company received $3.8 million and $0.7 million of funding under the grant for the year ended December 31, 2018 and 2017, respectively. The Company

recorded a receivable to reflect unreimbursed, eligible costs incurred under the CARB-X agreements in the amount of $1.5 million and $0.2 million as of December 31, 2018 and December 31, 2017, respectively.

Collaboration Agreement

In July 2017, the Company entered into a collaboration agreement (the "Agreement") with the Global Antibiotic Research and Development Partnership Drugs for Neglected Disease Initiative ("GARDP") for the development, manufacture and commercialization of a product candidate containing zoliflodacin in certain countries. The Phase 3 clinical trial has not commenced and there have been no material transactions with respect to the agreement as of December 31, 2018.

The Company also had zoliflodacin program activities conducted and funded by the U.S. government through its arrangements with the U.S. National Institute of Allergy and Infectious Diseases, or NIAID.

8. License and Collaboration Agreement with Zai Lab

In April 2018, the Company entered into a license and collaboration agreement with Zai Lab, pursuant to which Zai Lab licensed exclusive rights to ETX2514 and ETX2514SUL in the Asia-Pacific region (the "Zai Agreement"). Under the terms of the Zai Agreement, Zai Lab will fund most of the Company's clinical trial costs in China for ETX2514SUL, including all costs in China for the Company's planned Phase 3 clinical trial of ETX2514SUL, with the exception of patient drug supply. Zai Lab will conduct development activities, plan and obtain regulatory approval in a specified number of countries in the Asia-Pacific region beyond China after regulatory approval of a licensed product in China. Zai Lab is also solely responsible for commercializing licensed products in the Asia-Pacific region and will commercialize licensed products for which it has obtained regulatory approval. The Company is obligated to conduct specified development activities for the Asia-Pacific region. The Company is also obligated to supply Zai Lab with the licensed products for clinical development, although Zai Lab may take over manufacturing responsibilities for its own commercialization activities within a specified time period following the effective date of the Zai Agreement. Both parties are prohibited from developing and commercializing products in the Asia-Pacific region that would compete with the licensed products.

In addition, under the Zai Agreement, either party may propose that Zai Lab pursue a combination of imipenem together with ETX2514SUL in the territory. If the parties decide to pursue an imipenem combination, Zai Lab would provide the Company with limited research and development support for the combination.

The Company received an upfront, non-refundable payment of $5.0 million, less applicable taxes of $0.8 million, and $0.3 million of research support funding, less applicable taxes, from Zai Lab in 2018. The Company is eligible to receive up to an aggregate of $98.3 million in additional research and development support payments and development, regulatory and sales milestone payments related to ETX2514SUL, imipenem and other combinations with the licensed products. In the event the China Food and Drug Administration requires a modification or supplement to the trial protocol, and the Company delays Zai Lab from providing the required information and subsequently from obtaining regulatory approval for the pivotal study of ETX2514SUL in China, then the sales-based milestone payments that become due to the Company will be reduced by an agreed amount that increases with the length of the delay. Zai Lab will pay the Company a tiered royalty equal to a high-single digit to low-double digit percentage based on annual net sales of licensed products in the territory, subject to specified reductions for the market entry of competing products, loss of patent coverage of licensed products and for payments owed to third parties for additional rights necessary to commercialize licensed products in the territory.

The Company evaluated the Zai Agreement under Topic 606 and identified two material promises: (1) an exclusive license to develop, manufacture and commercialize products containing ETX2514 or ETX2514SUL in the territory and (2) the initial technology transfer of licensed know-how. The Company determined that the exclusive license and initial technology transfer were not distinct from one another, as the license has limited value without the transfer of the Company's technology and Zai Lab would incur additional costs to recreate the Company's know-how. Therefore, the license and initial technology transfer were combined as a single performance obligation.

The Company determined the $5.0 million non-refundable upfront payment is the entire transaction price at the outset of the Zai Agreement. All other future potential milestone payments were excluded from the transaction price as they are fully constrained as the risk of significant reversal has not yet been resolved. The achievement of the future potential milestones is not within the Company's control and is subject to certain research and development success, regulatory approvals or commercial success and therefore carry significant uncertainty. The Company will reevaluate the likelihood of achieving future milestones at the end of each reporting period. Future development milestone revenue from the arrangement will be recognized as revenue in the period when it is no longer probable that revenue attributable to the milestone will result in a significant reversal of cumulative revenue.

The Company delivered the exclusive license and performed the initial technology transfer of licensed know-how prior to June 30, 2018. The Company recognized $5.0 million of revenue for the year ended December 31, 2018. Additionally, the Company recorded a provision for income taxes of $0.5 million for the year ended December 31, 2018, associated with China withholding taxes on the upfront payment under the Zai Agreement.

9. Redeemable Convertible Preferred Stock

On September 28, 2018, upon the closing of the Company's IPO, all of the outstanding shares of Redeemable Convertible Preferred Stock ("Preferred Stock") of the Company automatically converted into 8,084,414 shares of the Company's common stock, which included 609,484 shares of the Company's common stock as settlement of the accrued dividends through September 27, 2018.

As of December 31, 2017, the Preferred Stock consisted of the following (in thousands, except share amounts):

	December 31, 2017			
	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation and Redemption Value	Common stock Issuable Upon Conversion
A Preferred Stock	33,499,900	$ 23,866	$ 37,039	1,616,166
B Preferred Stock	25,000,000	24,550	26,759	1,206,096
B-1 Preferred Stock	96,440,678	56,297	57,330	4,652,668
	154,940,578	$ 104,713	$ 121,128	7,474,930

The rights and privileges of the preferred stockholders were as follows:

Voting Rights

The Preferred Stock each had one vote for each share of common stock into which the share of Preferred Stock was convertible on a one-to-one basis. Preferred Stock and common stock voted together as a single class.

In the event that the shares of A Preferred Stock would constitute greater than 50% of the common stock (on an as-converted basis), then the A Preferred Stock, as a class, would have votes equal to 49% of the common stock (on an as-converted basis) and the voting rights attaching to each of the A Preferred Stock would accordingly be reduced on a pro-rata basis.

Distributions

Preferred stockholders were entitled to receive, when and if declared by the board of directors, out of any funds legally available, dividends at the rate of 4% of the original issue price per share. On September 28, 2018, the Company completed its initial public offering and issued an aggregate of 609,484 shares of its common stock as settlement of the

accrued dividends through September 27, 2018 due to the holders of Preferred Stock. No dividends accrue after September 27, 2018.

Liquidation Preference

Prior to the IPO, in the event of a Deemed Liquidation Event (as defined below), holders of the B-1 Preferred Stock then outstanding would have been entitled to be paid an amount equal to the greater of (a) $0.59 per share plus cumulative dividends, whether or not declared by the Company's board of directors, prior to any payment to the holders of the B Preferred Stock, A Preferred Stock and common shareholders or (b) the amount per share as would have been payable to the holders of the B-1 Preferred Stock had the conversion of the B-1 Preferred Stock into common stock taken place immediately prior to the date of the Deemed Liquidation Event (taking into account the conversion of all series of the Preferred Stock simultaneously).

Next, the holders of the B Preferred Stock then outstanding would be entitled to be paid an amount equal to the greater of (a) $1.00 per share plus cumulative dividends, whether or not declared by the Company's board of directors, prior to any payment to the holders of the A Preferred Stock and common shareholders or (b) the amount per share as would have been payable to the holders of the B Preferred Stock had the conversion of the B Preferred Stock into common stock taken place immediately prior to the date of the Deemed Liquidation Event (taking into account the conversion of all series of the Preferred Stock simultaneously).

Next, the holders of the A Preferred Stock then outstanding would be entitled to be paid an amount equal to the greater of (a) $1.00 per share plus cumulative dividends, whether or not declared by the Company's board of directors, prior to any payment to the common shareholders or (b) the amount per share as would have been payable to the holders of the A Preferred Stock had the conversion of the A Preferred Stock into common stock taken place immediately prior to the date of the Deemed Liquidation Event (taking into account the conversion of all series of Preferred Stock simultaneously).

After payment to the holders of the Preferred Stock, any remaining assets of the Company available for distribution to its shareholders would have been distributed among the common shareholders pro rata based on the number of shares held by each such holder.

A Deemed Liquidation Event was defined as (a) the appointment of a receiver or administrative receiver; (b) an administration order having been made; (c) the Company having stopped or suspended payment of its debts, becoming unable to pay its debts or otherwise becoming insolvent; (d) an unsatisfied judgement, order or award being outstanding against the Company; (e) the sale or transfer of the subsidiary to a third party; (f) the sale, transfer, exclusive license or other distribution of all or substantially all of the assets of the Company; (g) any consolidation or merger of the Company with or into any other corporation or other entity or person, or any other corporate reorganization, other than: any such consolidation, merger or reorganization in which the shares in issue immediately prior to such event continue to represent a majority of the voting power in the surviving entity immediately after such event; (h) any transaction or series of related transactions in which in excess of 50% of the voting power attaching to the shares in issue immediately prior to such transaction is transferred to a third party other than a direct or indirect wholly owned subsidiary of AstraZeneca; or (i) any other voluntary or involuntary dissolution, liquidation or winding up of the Company.

Conversion

The holders of the Preferred Stock had the following rights with respect to the conversion into common stock:

- The Preferred Stock was convertible at the option of the holder, at any time into common stock on a one-for-20.728 basis. These rights terminated in the event of a change in control, Deemed Liquidation Event, or termination by the Company without cause.

- All Preferred Stock would be automatically converted into common stock upon: (i) a public offering on the official list of the United Kingdom Listing Authority at a per share purchase price of at least two times the original purchase price of the B-1 Preferred Stock; (ii) a public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, resulting in at least $50.0 million of gross proceeds to the Company; or (iii) the election of 51% of the holders of outstanding Preferred Stock.

Redemption

The Preferred Stock was redeemable upon the occurrence of a Deemed Liquidation Event, which was not solely in control of the Company. Therefore, the Preferred Stock was classified as temporary equity at December 31, 2017.

10. Common Stock

As of December 31, 2018 and 2017, the Company's certificate of incorporation authorized the Company to issue 125,000,000 and 250,000,000 shares, respectively, of $0.001 par value common stock.

Each holder of common stock shall be entitled to one vote for each share of common stock held of record by such holder on all matters on which stockholders generally are entitled to vote. Common stockholders are entitled to receive dividends when and if declared by the board of directors, out of any funds legally available. As of December 31, 2018, no dividends have been declared or paid.

In September 2018, the Company's board of directors and stockholders approved, and the Company filed, an Amended and Restated Certificate of Incorporation effecting a 1-for-20.728 reverse stock split of its issued and outstanding common stock. All common share and per share data included in the consolidated financial statements reflect the reverse stock split.

On September 28, 2018, the Company completed an initial public offering in which the Company issued and sold 5,000,000 shares of its common stock, at a public offering price of $15.00 per share, for gross proceeds of $75.0 million. The Company received approximately $65.6 million in net proceeds after deducting underwriting discounts and commissions and offering costs. In connection with this financing, all outstanding shares of Preferred Stock, including accrued dividends, converted into 8,084,414 shares of the Company's common stock.

11. Stock-Based Compensation Expense

Stock Incentive Plan

In connection with the Reorganization, Entasis Therapeutics Holdings Inc. assumed the Entasis Limited amended and restated stock incentive plan, and each outstanding share option to purchase ordinary shares of Entasis Limited was assumed by Entasis Therapeutics Holdings Inc. and converted into an option to purchase the same number of shares of common stock of Entasis Therapeutics Holdings Inc. at the same exercise price per share and on the same vesting schedule. Each new option has and is subject to the same terms and conditions as were in effect immediately prior to the assumption and conversion. No share options of Entasis Limited are outstanding following the assumption and conversion.

In September 2018, the Company's board of directors adopted and its stockholders approved the 2018 Equity Incentive Plan (the "2018 Plan"), which became effective on September 25, 2018, at which point no further grants will be made under the 2015 Stock Incentive Plan (the "2015 Plan"). Under the 2018 Plan, the Company may grant incentive stock options ("ISOs"), non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. As of December 31, 2018, options to purchase an aggregate of 243,106 shares had been granted and 947,389 shares were available for future issuance under the 2018 Plan. The options issued under the 2018 Plan expire after 10 years.

ENTASIS THERAPEUTICS HOLDINGS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

Initially, subject to adjustment as provided in the 2018 Plan, the aggregate number of shares of the Company's common stock available for issuance under the 2018 Plan was 1,181,972. The number of shares of the Company's common stock reserved for issuance under the 2018 Plan will automatically increase on January 1 of each year, for a period of 10 years, from January 1, 2019 continuing through January 1, 2028, by 4% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by the Company's board of directors. The maximum number of shares that may be issued pursuant to the exercise of ISOs under the 2018 Plan is 7,500,000.

The maximum number of shares of the Company's common stock subject to awards granted under the 2018 Plan or otherwise during a single calendar year to any nonemployee directors, taken together with any cash fees paid by the Company to such nonemployee director during the calendar year for serving on the Company's board of directors, will not exceed $500,000 in total value, or, with respect to the calendar year in which a nonemployee director is first appointed or elected to the Company's board of directors, $800,000.

All options and awards granted under the 2015 Plan consisted of the Company's common stock. As of September 25, 2018, no additional stock awards have been or will be granted under the 2015 plan. Although the 2015 Plan was terminated as to future awards in September 2018, it continues to govern the terms of options that remain outstanding under the 2015 Plan.

Stock Option Activity

Stock option activity under both plans for year ended December 31, 2018 is summarized as follows:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2017	811,627	$ 3.73	9.09	$ 6,062
Granted	606,349	10.12		
Exercised	(27,789)	3.48		
Cancelled or forfeited	(14,457)	4.35		
Outstanding as of December 31, 2018	1,375,730	$ 6.54	8.66	$ 426
Vested or expected to vest at December 31, 2018	1,375,730	$ 6.54	8.66	$ 426
Exercisable at December 31, 2018	492,995	$ 4.54	7.86	$ 152

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the options and the fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock.

During the year ended December 31, 2018 and 2017 the weighted-average grant date fair value per granted option was $6.22 and $3.75, respectively.

Employee Stock Purchase Plan

In September 2018, the Company's board of directors and its stockholders approved the 2018 Employee Stock Purchase Plan (the "ESPP"), which became effective as of September 25, 2018. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the U.S. Internal Revenue Code of 1986, as amended. The number of shares of common stock initially reserved for issuance under the ESPP was 140,000 shares. The ESPP provides for an annual increase on the first day of each year beginning in 2019 and ending in 2028, in each case subject to the approval of the board of directors, equal to the lesser of (i) 1% of the shares of common stock outstanding on the last day of the prior fiscal year or (ii) 250,000 shares; provided, that prior to the date of any such

increase, the board of directors may determine that such increase will be less than the amount set forth in clauses (i) and (ii). As of December 31, 2018, no shares of common stock had been issued under the ESPP and 140,000 shares remained available for future issuance under the ESPP. No offering period under the ESPP has been set by the Company's board of directors.

AstraZeneca Shares Option and Incentive Plan

Certain employees of the Company participated in the AstraZeneca Shares Option and Incentive Plan (the "AstraZeneca Plan"), whereby employees of the Company continue to vest in the restricted shares ("AstraZeneca RSUs") of AstraZeneca ordinary shares issued by AstraZeneca to the employees prior to employment by the Company. AstraZeneca RSUs vested 100% after 36 months and were fully vested in March 2017 and therefore stock-based compensation expense for the AstraZeneca RSUs was recognized in full by September 30, 2017. The Company recorded stock-based compensation expense for AstraZeneca RSUs of $14,604 during the year ended December 31, 2017.

Stock-Based Compensation

Stock-based compensation expense was classified in the consolidated statement of operations as follows (in thousands):

	Year Ended December 31,	
	2018	2017
Research and development	$ 479	$ 229
General and administrative	722	191
Total stock-based compensation expense	$ 1,201	$ 420

As of December 31, 2018, total unrecognized stock-based compensation expense related to unvested options was $4.5 million, which is expected to be recognized over the weighted average period of approximately 2.8 years. The total unrecognized stock-based compensation expense will be adjusted for actual forfeitures as they occur.

The following weighted-average assumptions were used to calculate the fair value of each stock-based option award under the Black-Scholes option-pricing model:

	Year Ended December 31,	
	2018	2017
Expected stock price volatility	65.8 %	65.6 %
Risk-free interest rate	3.0 %	2.2 %
Expected annual dividend yield	—	—
Expected life of options	6.1 years	6.1 Years

12. Income Taxes

During the years ended December 31, 2018 and 2017, the Company recorded no income tax benefits for the net operating losses incurred due to its uncertainty of realizing a benefit from those items.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

Net loss before the provision for income taxes for the years ended December 31, 2018 and 2017, consisted of the following (in thousands):

	Year Ended December 31,	
	2018	2017
United Kingdom	$ 28,123	$ 21,806
United States	4,357	8,117
	$ 32,480	$ 29,923

As discussed in Note 1, on April 23, 2018, Entasis Limited completed a Reorganization resulting in Entasis Therapeutics Holdings Inc. becoming the sole shareholder of Entasis Limited. Upon the completion of the Reorganization, the historical consolidated financial statements of Entasis Limited became the historical consolidated financial statements of Entasis Therapeutics Holdings Inc. As a result of this Reorganization, the reconciliation below of statutory income tax rates to the Company's effective income tax rates is based on U.S. statutory rates in 2018 and U.K. statutory rates in 2017:

	Year Ended December 31,	
	2018	2017
Income tax benefit computed at statutory tax rate	21.0 %	19.0 %
State taxes, net of federal benefit	4.6	1.3
Foreign rate differential	(3.4)	4.1
Research and development tax credits	1.4	3.0
Permanent difference	11.5	(1.3)
Valuation allowances	(35.1)	(17.7)
Rate changes	—	(8.4)
Foreign withholding tax	(1.4)	—
Effective income tax rate	(1.4)%	(0.0)%

The Company recorded a tax provision of $0.5 million in 2018 associated with China withholding taxes on the upfront payment under the Zai Agreement.

Net deferred tax assets as of December 31, 2018 and 2017 consisted of the following (in thousands):

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$ 20,051	$ 8,967
Tax credit carryforwards	2,321	1,763
Depreciation and amortization	—	7
Accrued expenses and other	1,097	987
Total deferred tax assets	23,469	11,724
Depreciation and amortization	(10)	—
Total deferred tax liabilities	(10)	—
Valuation allowance	(23,459)	(11,724)
Net deferred tax assets	$ —	$ —

ENTASIS THERAPEUTICS HOLDINGS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2018 and 2017 related primarily to the increases in NOLs and research and development tax credit carryforwards and were as follows (in thousands):

	Year Ended December 31,	
	2018	2017
Valuation allowance at beginning of year	$ (11,724)	$ (6,415)
Increases recorded to income tax provision	(11,735)	(5,309)
Valuation allowance at end of year	$ (23,459)	$ (11,724)

On December 22, 2017, the President of the United States signed into law the Tax Cuts and Jobs Act ("TCJA") tax reform legislation. The legislation reduced the U.S. corporate tax rate from the current rate of 35% down to 21% effective for tax years beginning after December 31, 2017. As a result of the TCJA, at December 31, 2017 the Company revalued deferred tax assets and liabilities at the new rate. This revaluation resulted in a reduction in deferred tax assets of $1.7 million with a corresponding reduction in the valuation allowance. There was no impact to the Company's statement of operations as a result of a reduction in tax rate.

Also as a result of passage of the TCJA, net operating losses generated in years ending after December 31, 2018 will be carried forward indefinitely and can no longer be carried back, and net operating losses generated in years beginning after December 31, 2017, can only reduce taxable income by 80% when utilized in a future period. The exact ramifications of the legislation are subject to interpretation and could have a material impact on the Company's financial position and/or results of operations. The TCJA is complex and far-reaching, and its effect, whether adverse or favorable, may not become evident for some period of time.

As of December 31, 2018, the Company had U.S. federal and state net operating loss carryforwards ("NOLs") of $33.8 million and $34.5 million, respectively, which begin to expire in 2035. Included in the $33.8 million of federal net operating losses are losses of $21.2 million that will carry forward indefinitely as a result of the Tax Cuts and Jobs Act. As of December 31, 2018, the Company had federal and state research and development tax credits carryforwards of $1.8 million and $0.7 million, which begin to expire in 2035 and 2026, respectively.

Utilization of the U.S. federal NOLs and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the shares of a corporation by more than 50% over a three-year period. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception, due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the NOLs or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's shares at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the NOLs or research and development tax credit carryforwards before utilization.

As of December 31, 2018, the Company had NOLs in the United Kingdom of $63.3 million to offset future taxable income. The NOLs in the United Kingdom can be carried forward indefinitely.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of its deferred tax assets.

Accordingly, a full valuation allowance of $23.5 million has been established against the deferred tax assets as of December 31, 2018.

The Company has not recorded an amount for unrecognized tax benefits or related interest and penalties accrued as of December 31, 2018. The Company files income tax returns in the United States, Massachusetts and the United Kingdom. The U.S. federal and state returns are generally subject to tax examinations for the tax years ended December 31, 2015 to the present. The statute of limitations for assessment by the United Kingdom is open for the tax years since 2015. There are currently no pending tax examinations. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service and state tax authorities to the extent utilized in a future or prior period. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision.

13. Net Loss per Share

Basic and diluted net loss per share of the Company was calculated as follows (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2018	2017
Numerator:		
Net loss	$ (32,952)	$ (29,923)
Less: Dividends declared	(9,142)	—
Net loss attributable to common stockholders—basic and diluted	$ (42,094)	$ (29,923)
Denominator:		
Weighted average common stock outstanding—basic and diluted	3,419,720	2,169
Net loss per share attributable to common stockholders—basic and diluted	$ (12.31)	$ (13,795.76)

The Company excluded the following potential shares of common stock, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect. Therefore, the weighted average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same.

	As of December 31,	
	2018	2017
Options to purchase shares of common stock	1,375,730	811,627
Redeemable convertible preferred stock (as converted to common stock)	—	7,474,930
	1,375,730	8,286,557

14. Commitments

Lease Commitments

In May 2015, the Company entered into an operating lease agreement for its office and laboratory space with AstraZeneca, which extended through May 2020. In February 2018, the Company amended its operating lease to extend the term through December 2022 and expand the premises to include an additional 7,257 square feet. The facility lease requires the Company to pay certain operating costs. During the year ended December 31, 2018 and 2017, the Company recorded rental expense of $0.6 million and $0.4 million, respectively.

Future minimum lease payments for the combined spaces as of December 31, 2018 were as follows (in thousands):

Year Ending December 31,	
2019	$ 597
2020	656
2021	710
2022	730
	$ 2,693

A Subscription Agreement

In connection with the A Subscription Agreement, the Company agreed to pay AstraZeneca a one-time milestone payment of $5.0 million within three months of achieving a specified cumulative net sales milestone for ETX2514. This milestone payment will be automatically waived should the Company's common stock trade on Nasdaq at or above a specified price at the time it achieves such specified cumulative net sales milestone for ETX2514. The Company is also obligated to pay AstraZeneca a one-time milestone payment of $10.0 million within two years of achieving the first commercial sale of zoliflodacin. At the Company's election, either milestone payment may be paid in cash, common stock, or a combination of cash and common stock. Additionally, the Company is obligated to pay AstraZeneca tiered, single-digit, per-country royalties on the annual worldwide net sales of ETX2514 and zoliflodacin.

15. Related Party Transactions

The Company was formed in May 2015 as a wholly owned subsidiary of AstraZeneca, which maintained a controlling interest in the Company until the B Preferred Stock were issued in March 2016. Prior to the closing of the initial public offering on September 28, 2018, AstraZeneca was the sole A Preferred Stockholder. Upon the closing of the initial public offering, all shares of preferred stock converted into shares of common stock.

Subscription Receivable Due from AstraZeneca

In connection with the issuance and sale of A Preferred Stock, AstraZeneca agreed to provide cash management services for the net proceeds due to the Company under the A Preferred Stock financing for as long as the Company remained a majority-controlled subsidiary. As a result, the full amount of the funds due to the Company were held by AstraZeneca, as property of the Company. This arrangement ceased upon the closing the B Preferred Stock financing in March 2016. During 2016, $17.6 million of the funds were transferred to the Company, with the remaining $0.2 million received in 2017.

Lease Commitments

The Company has an operating lease agreement for its office and laboratory space with AstraZeneca. See Note 14.

16. Benefit Plans

The Company has a tax-qualified employee savings and retirement 401(k) plan, covering all qualified employees. Participants may elect a salary deferral up to the statutorily prescribed annual limit for tax-deferred contributions. The Company made matching contributions of $0.2 million and $0.1 million for each of the years ended December 31, 2018 and 2017, respectively.

EMPLOYMENT AGREEMENT

This **EMPLOYMENT AGREEMENT** (this "***Agreement***") is entered into as of September 25, 2018, by and between Ruben Tommasi ("***Executive***") and Entasis Therapeutics Holdings Inc. (the "***Company***"), and which shall become effective upon the effectiveness of the registration statement for the Company's initial public offering (the "***Effective Date***").

Executive previously entered into an Offer Letter with the Company effective as of May 11, 2015, as amended on August 28, 2017 (the "***Prior Agreement***");

The parties desire to amend, restate and replace the Prior Agreement;

The Company desires to continue to employ Executive and, in connection with such employment, to compensate Executive for Executive's personal services to the Company; and

Executive desires to continue to be employed by the Company and to provide personal services to the Company in return for certain compensation.

Accordingly, in consideration of the mutual promises and covenants contained herein, the parties agree to the following:

1. EMPLOYMENT BY THE COMPANY.

1.1 At-Will Employment. Executive will continue to be employed by the Company on an "at-will" basis, meaning either the Company or Executive may terminate Executive's employment at any time, with or without cause or advanced notice. Any contrary representations that may have been made to Executive are superseded by this Agreement. This Agreement is the full and complete agreement between Executive and the Company on the "at-will" nature of Executive's employment with the Company, which may be changed only in an express written agreement signed by Executive and a duly authorized officer of the Company. Executive's rights to any compensation following a termination are only as set forth in Section 6.

1.2 Position. Subject to the terms of this Agreement, the Company agrees to continue to employ Executive, as Chief Scientific Officer, and Executive hereby accepts such continued employment. During the term of Executive's employment with the Company, Executive will devote Executive's best efforts and substantially all of Executive's business time and attention to the business of the Company.

1.3 Duties. As Chief Scientific Officer, Executive will report to the Chief Executive Officer (the "***CEO***") performing such duties as are normally associated with Executive's position and such duties as are assigned to Executive from time to time by the CEO, subject to the oversight and direction of the CEO. Executive will perform Executive's duties under this Agreement principally out of the Company's corporate headquarters. In addition, Executive will make such business trips to such places as may be necessary or advisable for the efficient operations of the Company.

1.4 Company Policies and Benefits. The employment relationship between the parties is also subject to the Company's personnel and compliance policies and procedures as

they may be interpreted, adopted, revised or deleted from time to time in the Company's sole discretion. Executive will continue to be eligible to participate on the same basis as similarly situated executives in the Company's benefit plans in effect from time to time during Executive's employment. All matters of eligibility for coverage or benefits under any benefit plan will be determined in accordance with the provisions of the plan. The Company reserves the right to change, alter, or terminate any benefit plan in its sole discretion. Notwithstanding the foregoing, in the event that the terms of this Agreement differ from, or are in conflict with, the Company's general employment policies or practices, this Agreement will control.

2. COMPENSATION.

2.1 Salary. Executive will receive for Executive's services to be rendered hereunder an initial annualized base salary of US$311,042, subject to review and adjustment from time to time by the Company in its sole discretion, payable subject to standard payroll withholding requirements in accordance with Company's standard payroll practices ("***Base Salary***").

2.2 Bonus. While this Agreement is in effect, Executive will continue to be eligible for a discretionary annual cash bonus with a target of thirty-five percent (35%) of Executive's then current Base Salary, subject to review and adjustment from time to time by the Company in its sole discretion, payable subject to standard payroll withholding requirements ("***Target Bonus***"). Whether or not Executive earns any bonus will be dependent upon (a) the actual achievement by Executive and the Company of the applicable individual and corporate performance goals, as determined by the Board of Directors of the Company (the "***Board***") in its sole discretion, and (b) Executive's continuous performance of services to the Company through December 31 of the year any bonus may be earned. The bonus may be greater or lesser than the Target Bonus and may be zero. In all events, any bonus earned pursuant to this Section 2.2 will be paid on or before March 15 of the year following the year for which it is earned.

2.3 Equity. Executive has been granted options to purchase shares of the Company's Common Stock (the "**Options**"), the terms of which will continue to be governed in all respects by the governing plan documents, grant notices and stock option agreements. Executive will be eligible to receive further stock grants and/or stock option awards in the sole discretion of the Board or its Compensation Committee.

2.4 Expense Reimbursement. The Company will reimburse Executive for reasonable business expenses with proper documentation and in accordance with the Company's standard expense reimbursement policy. For the avoidance of doubt, to the extent that any reimbursements payable to Executive are subject to the provisions of Section 409A of the Internal Revenue Code of 1986, as amended (the "***Code***"): (a) any such reimbursements will be paid no later than December 31 of the year following the year in which the expense was incurred, (b) the amount of expenses reimbursed in one year will not affect the amount eligible for reimbursement in any subsequent year, and (c) the right to reimbursement under this Agreement will not be subject to liquidation or exchange for another benefit.

3. CONFIDENTIALITY AND PROPRIETARY RIGHTS OBLIGATIONS. The parties have entered into a Confidentiality & Proprietary Rights Agreement and a Restrictive Covenant (collectively, "***Confidential Information Agreement***"), which may be amended by the parties

from time to time without regard to this Agreement. The Confidential Information Agreement contains provisions that are intended by the parties to survive and do survive termination or expiration of this Agreement.

4. OUTSIDE ACTIVITIES DURING EMPLOYMENT. Except with the prior written consent of the Chairman of the Board and the Company's CEO, Executive will not, while employed by the Company, undertake or engage in any other employment, occupation or business enterprise that would interfere with Executive's responsibilities and the performance of Executive's duties hereunder except for (i) reasonable time devoted to volunteer services for or on behalf of such religious, educational, non-profit and/or other charitable organization as Executive may wish to serve, (ii) reasonable time devoted to activities in the non-profit and business communities consistent with Executive's duties, and (iii) such other activities as may be specifically approved by the Chairman of the Board and the CEO. This restriction will not, however, preclude Executive (x) from owning less than one percent (1%) of the total outstanding shares of a publicly traded company, or (y) from employment or service in any capacity with Affiliates of the Company. As used in this Agreement, "***Affiliates***" means an entity under common management or control with the Company. Notwithstanding this Section 4, the Chairman of the Board and the CEO will continue to permit Executive to serve as a board member of one (1) other company or entity, such company or entity whose identity Executive has disclosed or will disclose to the Chairman of the Board and the CEO, unless such company or entity is reasonably deemed by the Chairman of the Board and the CEO to be competitive with the Company, and further provided that Executive's service as a board member of that company or entity will not in any way materially limit or adversely impact Executive's compliance with the duties and obligations that Executive has and owes to the Company, including under this Agreement or the Confidential Information Agreement.

5. NO CONFLICT WITH EXISTING OBLIGATIONS. Executive represents that Executive's performance of all the terms of this Agreement and as an Executive of the Company does not and will not breach any agreement or obligation of any kind made prior to Executive's employment by the Company, including agreements or obligations Executive may have with prior employers or entities for which Executive has provided services. Executive has not entered into, and Executive agrees that Executive will not enter into, any agreement or obligation, either written or oral, in conflict with his obligations under this Agreement.

6. TERMINATION OF EMPLOYMENT. Executive and the Company each acknowledge that, pursuant to Section 1 of this Agreement, either party has the right to terminate Executive's employment with the Company at any time for any reason whatsoever, with or without cause or advance notice. The provisions in this Section 6 govern the amount of compensation, if any, to be provided to Executive upon termination of employment and do not alter this at-will status.

6.1 Termination by the Company without Cause or Resignation by Executive for Good Reason (Other Than in Connection with a Change in Control).

(a) The Company will have the right to terminate Executive's employment with the Company at any time without Cause (as defined below). Likewise, Executive may resign for Good Reason (as defined below). In the absence of a Change in Control

(as defined below) and in the event Executive is terminated by the Company without Cause, but not in the event of a termination due to death or Disability under Section 6.4, or Executive resigns for Good Reason (as defined below), then Executive will be entitled to receive the Accrued Obligations (as defined below) and in addition, provided such termination constitutes a "separation from service" (as defined under Treasury Regulation Section 1.409A-1(h), without regard to any alternative definition thereunder, a "***Separation from Service***"), and further provided Executive complies with the obligations in Section 6.1(b) below, Executive will also be eligible to receive the following "***Severance Benefits***":

(i) The Company will pay Executive an amount equal to Executive's then current Base Salary for twelve (12) months, less standard withholdings and deductions, paid in installments on the Company's regular payroll dates.

(ii) If Executive is participating in the Company's group health plans as of the date of termination, and if Executive timely elects continued coverage under COBRA or, if applicable, state continuation coverage laws, the Company will pay the premiums necessary to continue Executive and Executive's covered dependents' health insurance coverage in effect on the termination date until the earliest of: (i) twelve (12) months following the termination date; (ii) the date when Executive becomes eligible for health insurance coverage in connection with new employment or self-employment; or (iii) the date Executive ceases to be eligible for continuation coverage for any reason, including plan termination (such period from the termination date through the earlier of (i)-(iii), (the "***COBRA Payment Period***"). Notwithstanding the foregoing, if at any time the Company determines that its payment of continuation coverage premiums on Executive's behalf would result in a violation of applicable law (including, but not limited to, the 2010 Patient Protection and Affordable Care Act, as amended by the 2010 Health Care and Education Reconciliation Act), then in lieu of paying premiums pursuant to this Section, the Company will pay Executive on the last day of each remaining month of the COBRA Payment Period, a fully taxable cash payment equal to the premium it would have paid for such month, subject to applicable tax withholding (such amount, the "***Special Severance Payment***"), for the remainder of the COBRA Payment Period.

(b) Executive will receive the Severance Benefits pursuant to Section 6.1(a) of this Agreement if: (i) within the timeframe provided by the Company, Executive has signed and delivered to the Company a separation agreement containing an effective, general release of claims in favor of the Company and its affiliates and representatives, in a form presented by the Company (the "***Release***"), which cannot be revoked in whole or part by such date (the date that the Release can no longer be revoked is referred to as the "***Release Effective Date***"); and (ii) if Executive holds any other positions with the Company or any affiliate, including a position on the Board, Executive resigns such position(s) to be effective no later than the date of Executive's Separation from Service (or such other date as requested by the Board); (iii) Executive returns all Company property; (iv) Executive complies with Executive's post-termination obligations under this Agreement and the Confidential Information Agreement; and (v) Executive complies with the terms of the Release, including without limitation any non-disparagement and confidentiality provisions contained in the Release.

(c) The Company will not make any payments to Executive with respect to any of the benefits pursuant to Section 6.1(a) prior to the 60th day following Executive's date of termination. On the 60th day following Executive's date of termination, and provided that Executive has delivered an effective Release, the Company will make the first payment to Executive under Section 6.1(a)(i) in a lump sum equal to the aggregate amount of payments that the Company would have paid Executive through such date had the payments commenced on Executive's date of termination through such 60th day, with the balance of the payments paid thereafter on the schedule described above.

(d) For purposes of this Agreement, "***Accrued Obligations***" are (i) Executive's accrued but unpaid salary through the date of termination, (ii) any unreimbursed business expenses incurred by Executive payable in accordance with the Company's standard expense reimbursement policies, (iii) benefits owed to Executive under any qualified retirement plan or health and welfare benefit plan in which Executive was a participant in accordance with applicable law and the provisions of such plan, and (iv) Executive's accrued but unused vacation through the date of termination.

(e) The Severance Benefits provided to Executive pursuant to Section 6.1(a) are in lieu of, and not in addition to, any benefits to which Executive may otherwise be entitled under any Company severance plan, policy or program.

(f) Any damages caused by the termination of Executive's employment without Cause would be difficult to ascertain; therefore, the Severance Benefits for which Executive is eligible pursuant to Section 6.1(a) above in exchange for the Release is agreed to by the parties as liquidated damages, to serve as full compensation, and not a penalty.

(g) For purposes of this Agreement, "***Good Reason***" means any of the following actions taken by the Company without Executive's consent: (i) any material diminution of Executive's authority, duties or responsibilities; (ii) a material (greater than ten percent (10%)) reduction by the Company of Executive's Base Salary except in the case of across-the-board salary reductions based on the Company's financial performance similarly affecting all or substantially all similarly-situated employees of the Company; (iii) a relocation of Executive's place of employment to a location in excess of fifty (50) miles from the Company's current principal place of employment; (iv) any material breach of this Agreement by the Company; *provided, however,* that it will only be deemed Good Reason if (1) the Company has not previously notified Executive of its intention to terminate his employment; (2) the Company is given written notice from Executive within ninety (90) days following the first occurrence of a condition that Executive considers to constitute Good Reason (with such notice including a description of the condition); (3) the Company fails to remedy such condition within thirty (30) days following such written notice; and (4) Executive resigns from employment with the Company effective not later than thirty (30) days after the end of the Company's cure period. Notwithstanding the foregoing, any actions taken by the Company to accommodate a Disability of Executive or pursuant to the Family and Medical Leave Act or an applicable state leave law will not be a Good Reason for purposes of this Agreement.

6.2 Termination by the Company for Cause or Resignation by Executive (Other Than for Good Reason).

(a) If the Company terminates Executive's employment for Cause or Executive resigns from employment with the Company without Good Reason, regardless of whether or not such termination is in connection with a Change in Control, then Executive will be entitled to the Accrued Obligations, but Executive will not receive the Severance Benefits or any other severance compensation or benefit.

(b) "***Cause***" for termination will mean that the Board has determined in its sole discretion that Executive has engaged in any of the following: (i) a material breach of this Agreement or any other written agreement between Executive and the Company; (ii) gross negligence or gross misconduct in the performance of Executive's duties; (iii) the commission of any act or omission constituting dishonesty or fraud that is injurious to the Company or any affiliate thereof; (iv) any conduct which constitutes a felony under applicable law; (v) conduct by Executive which demonstrates gross unfitness to serve; (vi) failure to attempt in good faith to implement a clear, reasonable and legal directive of the Company's CEO, the Board or any Board committee; or (vii) breach of a fiduciary duty.

6.3 Change in Control Severance Benefits.

(a) In the event that the Company (or any surviving or acquiring corporation) terminates Executive's employment without Cause or Executive resigns for Good Reason on or within eighteen (18) months following the effective date of a Change in Control ("***Change in Control Termination***"), Executive will be entitled to the Accrued Obligations, and upon executing and allowing to become effective the Release, Executive will be eligible to receive the following Change in Control severance benefits:

(i) a lump-sum cash payment in an amount equal to twelve (12) months of Executive's Base Salary then in effect (the "***Lump Sum Severance***");

(ii) a lump-sum cash payment in an amount equal to one (1) times Executive's Target Bonus for the year in which Executive's employment terminates (the "***Bonus Severance***");

(iii) if Executive is participating in the Company's group health plans as of a Change in Control Termination, and if Executive timely elects continued coverage under COBRA or, if applicable, state continuation coverage laws, the Company will pay the premiums necessary to continue Executive and Executive's covered dependents' health insurance coverage in effect on the Change in Control Termination date until the earliest of: (A) twelve (12) months following a Change in Control Termination; (B) the date when Executive becomes eligible for health insurance coverage in connection with new employment or self-employment; or (C) the date Executive ceases to be eligible for continuation coverage for any reason, including plan termination, provided, however, if at any time the Company determines that its payment of continuation coverage premiums on Executive's behalf would result in a violation of applicable law (including, but not limited to, the 2010 Patient Protection and Affordable Care Act, as amended by the 2010 Health Care and Education Reconciliation Act), then in lieu of paying premiums

pursuant to this Section, the Company will pay Executive on the last day of each remaining month of the COBRA Payment Period, a fully taxable cash payment equal to the premium it would have paid for such month, subject to applicable tax withholding, for the remainder of the COBRA Payment Period; and

(iv) effective as of the later of Executive's Change in Control Termination date or the effective date of the Change in Control, the vesting and exercisability of all outstanding stock options and other stock awards covering the Company's Common Stock that are held by Executive as of immediately prior to the Change in Control Termination date, to the extent such awards are subject to time-based vesting requirements, will be accelerated (and lapse, in the case of reacquisition or repurchase rights) in full. Executive's stock options and stock awards will remain outstanding following Executive's Change in Control Termination date if and to the extent necessary to give effect to this Section 6.3(a)(iv) subject to earlier termination under the terms of the equity plan and award agreements under which such awards were granted and the original maximum term of the award (without regard to Executive's termination).

(b) To receive the payments and benefits under (a) above, Executive's termination or resignation must constitute a "separation from service" (as defined under Treasury Regulation Section 1.409A-1(h)) and Executive must execute and allow the Release to become effective within the time period provided by the Company, which shall be no later than 60 days following Executive's termination or resignation. The Lump Sum Severance and Bonus Severance will be paid, subject to deductions and withholdings, by the 60th day following Executive's termination or resignation, provided Executive has timely delivered the effective Release. For the avoidance of doubt, in the event of a Change in Control Termination, Executive only will be eligible to receive the severance benefits under this Section 6.3 and not those severance benefits under Section 6.1.

(c) For purposes of this Agreement, "***Change in Control***" will have the meaning ascribed to such term in the Company's 2018 Equity Incentive Plan.

6.4 Termination by Virtue of Death or Disability of Executive.

(a) In the event of Executive's death while employed pursuant to this Agreement, all obligations of the parties hereunder will terminate immediately. Executive's legal representatives will not receive the Severance Benefits, or any other severance compensation or benefit, except that, pursuant to the Company's standard payroll policies, the Company will provide to Executive's legal representatives the Accrued Obligations.

(b) Subject to applicable state and federal law, the Company will at all times have the right, upon written notice to Executive, to terminate this Agreement based on Executive's Disability (as defined below). Termination by the Company of Executive's employment based on "***Disability***" will mean termination because Executive is unable due to a physical or mental condition to perform the essential functions of Executive's position with or without reasonable accommodation for six (6) months in the aggregate during any twelve (12) month period or based on the written certification by two licensed physicians of the likely continuation of such condition for such period. This definition will be interpreted and applied consistent with the Americans with Disabilities Act, the Family and Medical Leave Act, and other

applicable law. In the event Executive's employment is terminated based on Executive's Disability, Executive will not receive the Severance Benefits, or any other severance compensation or benefit, except that, pursuant to the Company's standard payroll policies, the Company will provide to Executive the Accrued Obligations.

6.5 Cooperation with the Company after Termination of Employment. Following termination of Executive's employment for any reason, Executive will fully cooperate with the Company in all matters relating to the winding up of Executive's pending work including, without limitation, any litigation in which the Company is involved or such other inquiry concerning the Company that Executive may have knowledge, the signing of routine documents for administrative or compliance purposes, announcements concerning termination and the orderly transfer of any pending work to such other executives or Executives as may be designated by the Company.

6.6 Section 409A.

(a) Notwithstanding anything to the contrary herein, the following provisions apply to the extent severance benefits provided herein are subject to Section 409A of the Internal Revenue Code (the "***Code***") and the regulations and other guidance thereunder and any state law of similar effect (collectively "***Section 409A***"). Severance benefits will not commence until Executive has a "separation from service" (as defined under Treasury Regulation Section 1.409A-1(h), without regard to any alternative definition thereunder, a "separation from service"). Each installment of severance benefits is a separate "payment" for purposes of Treas. Reg. Section 1.409A-2(b)(2)(i), and the severance benefits are intended to satisfy the exemptions from application of Section 409A provided under Treasury Regulations Sections 1.409A-1(b)(4), 1.409A-1(b)(5) and 1.409A-1(b)(9). Notwithstanding any provision to the contrary in this Agreement, if Executive is deemed by the Company at the time of Executive's separation from service to be a "specified employee" for purposes of Section 409A(a)(2)(B)(i) of the Code, and if any of the payments due upon separation from service set forth herein and/or under any other agreement with the Company are deemed to be "deferred compensation," then to the extent delayed commencement of any portion of such payments is required to avoid a prohibited distribution under Section 409A(a)(2)(B)(i) of the Code and the related adverse taxation under Section 409A, such payments will not be provided to Executive prior to the earliest of (i) the expiration of the six (6)-month period measured from the date of Executive's separation from service with the Company, (ii) the date of Executive's death or (iii) such earlier date as permitted under Section 409A without the imposition of adverse taxation. Upon the first business day following the expiration of such applicable Code Section 409A(a)(2)(B)(i) period, all payments deferred pursuant to this paragraph will be paid in a lump sum to Executive, and any remaining payments due will be paid as otherwise provided in this Agreement or in the applicable agreement. No interest will be due on any amounts so deferred. To the extent that any severance payments are deferred compensation under Section 409A, and are not otherwise exempt from the application of Section 409A, then, if the period during which Executive may consider and sign the Release spans two calendar years, the payment of severance will not be made or begin until the later calendar year. The parties acknowledge that the exemptions from application of Section 409A to severance benefits are fact specific, and any later amendment of this Agreement to alter the timing,

amount or conditions that will trigger payment of severance benefits may preclude the ability of severance benefits provided under this Agreement to qualify for an exemption.

(b) Notwithstanding anything in this Agreement to the contrary or otherwise, with respect to any expense, reimbursement or in-kind benefit provided pursuant to this Agreement that constitutes a "deferral of compensation" within the meaning of Section 409A and its implementing regulations and guidance, (a) the expenses eligible for reimbursement or in-kind benefits provided to Executive must be incurred during the term of the Agreement (or applicable survival period), (b) the amount of expenses eligible for reimbursement or in-kind benefits provided to Executive during any calendar year will not affect the amount of expenses eligible for reimbursement or in-kind benefits provided to Executive in any other calendar year, (c) the reimbursements for expenses for which Executive is entitled to be reimbursed shall be made on or before the last day of the calendar year following the calendar year in which the applicable expense is incurred and (d) the right to payment or reimbursement or in-kind benefits hereunder may not be liquidated or exchanged for any other benefit.

(c) It is intended that this Agreement will comply with the requirements of Section 409A, and any ambiguity contained herein will be interpreted in such manner so as to avoid adverse personal tax consequences under Section 409A. Notwithstanding the foregoing, the Company will in no event be obligated to indemnify Executive for any taxes or interest that may be assessed by the Internal Revenue Service pursuant to Section 409A of the Code to payments made pursuant to this Agreement.

6.7 Section 280G.

(a) If any payment or benefit Executive will or may receive from the Company or otherwise (a "***280G Payment***") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "***Excise Tax***"), then any such 280G Payment pursuant to this Agreement or otherwise (a "***Payment***") shall be equal to the Reduced Amount. The "Reduced Amount" shall be either (x) the largest portion of the Payment that would result in no portion of the Payment (after reduction) being subject to the Excise Tax or (y) the largest portion, up to and including the total, of the Payment, whichever amount (i.e., the amount determined by clause (x) or by clause (y)), after taking into account all applicable federal, state and local employment taxes, income taxes, and the Excise Tax (all computed at the highest applicable marginal rate), results in Executive's receipt, on an after-tax basis, of the greater economic benefit notwithstanding that all or some portion of the Payment may be subject to the Excise Tax. If a reduction in a Payment is required pursuant to the preceding sentence and the Reduced Amount is determined pursuant to clause (x) of the preceding sentence, the reduction shall occur in the manner (the "***Reduction Method***") that results in the greatest economic benefit for Executive. If more than one method of reduction will result in the same economic benefit, the items so reduced will be reduced pro rata (the "***Pro Rata Reduction Method***").

(b) Notwithstanding the foregoing, if the Reduction Method or the Pro Rata Reduction Method would result in any portion of the Payment being subject to taxes pursuant to Section 409A that would not otherwise be subject to taxes pursuant to Section 409A, then the Reduction Method and/or the Pro Rata Reduction Method, as the case may be, shall be modified

so as to avoid the imposition of taxes pursuant to Section 409A as follows: (A) as a first priority, the modification shall preserve to the greatest extent possible, the greatest economic benefit for Executive as determined on an after-tax basis; (B) as a second priority, Payments that are contingent on future events (e.g., being terminated without cause), shall be reduced (or eliminated) before Payments that are not contingent on future events; and (C) as a third priority, Payments that are "deferred compensation" within the meaning of Section 409A shall be reduced (or eliminated) before Payments that are not deferred compensation within the meaning of Section 409A.

(c) Unless Executive and the Company agree on an alternative accounting firm, the accounting firm engaged by the Company for general tax compliance purposes as of the day prior to the effective date of the change of control transaction triggering the Payment shall perform the foregoing calculations. If the accounting firm so engaged by the Company is serving as accountant or auditor for the individual, entity or group effecting the change in control transaction, the Company shall appoint a nationally recognized accounting firm to make the determinations required hereunder. The Company shall bear all expenses with respect to the determinations by such accounting firm required to be made hereunder. The Company shall use commercially reasonable efforts to cause the accounting firm engaged to make the determinations hereunder to provide its calculations, together with detailed supporting documentation, to Executive and the Company within fifteen (15) calendar days after the date on which Executive's right to a 280G Payment becomes reasonably likely to occur (if requested at that time by Executive or the Company) or such other time as requested by Executive or the Company.

(d) If Executive receives a Payment for which the Reduced Amount was determined pursuant to clause (x) of Section 6.7(a) and the Internal Revenue Service determines thereafter that some portion of the Payment is subject to the Excise Tax, Executive shall promptly return to the Company a sufficient amount of the Payment (after reduction pursuant to clause (x) of Section 6.7(a)) so that no portion of the remaining Payment is subject to the Excise Tax. For the avoidance of doubt, if the Reduced Amount was determined pursuant to clause (y) in Section 6.7(a), Executive shall have no obligation to return any portion of the Payment pursuant to the preceding sentence.

7. GENERAL PROVISIONS.

7.1 Notices. Any notices required hereunder to be in writing will be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by electronic mail or confirmed facsimile, if sent during normal business hours of the recipient, and if not, then on the next business day, (c) three (3) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of delivery. All communications will be sent to the Company at its primary office location and to Executive at Executive's then current address as listed in Company records, or at such other address as the Company or Executive may designate by ten (10) days advance written notice to the other.

7.2 Severability. Whenever possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be invalid, illegal or unenforceable in any respect under any applicable

law or rule in any jurisdiction, such invalidity, illegality or unenforceability will not affect any other provision or any other jurisdiction, but this Agreement will be reformed, construed and enforced in such jurisdiction as if such invalid, illegal or unenforceable provisions had never been contained herein.

7.3 Survival. Provisions of this Agreement which by their terms must survive the termination of this Agreement in order to effectuate the intent of the parties will survive any such termination, whether by expiration of the term, termination of Executive's employment, or otherwise, for such period as may be appropriate under the circumstances.

7.4 Waiver. If either party should waive any breach of any provisions of this Agreement, Executive or the Company will not thereby be deemed to have waived any preceding or succeeding breach of the same or any other provision of this Agreement.

7.5 Complete Agreement. This Agreement constitutes the entire agreement between Executive and the Company with regard to the subject matter hereof. This Agreement is the complete, final, and exclusive embodiment of their agreement with regard to this subject matter and supersedes any prior oral discussions or written communications and agreements, including the Prior Agreement. This Agreement is entered into without reliance on any promise or representation other than those expressly contained herein, and it cannot be modified or amended except in writing signed by Executive and an authorized officer of the Company. The parties have entered into a separate Confidential Information Agreement and may have entered into other agreements governing stock option(s) or other equity awards. Any such separate agreements govern other aspects of the relationship between the parties, have or may have provisions that survive termination of Executive's employment under this Agreement, may be amended or superseded by the parties without regard to this agreement and are enforceable according to their terms without regard to the enforcement provision of this Agreement.

7.6 Counterparts. This Agreement may be executed in separate counterparts, any one of which need not contain signatures of more than one party, but all of which taken together will constitute one and the same Agreement.

7.7 Headings. The headings of the sections hereof are inserted for convenience only and will not be deemed to constitute a part hereof nor to affect the meaning thereof.

7.8 Successors and Assigns. The Company will assign this Agreement and its rights and obligations hereunder in whole, but not in part, to any Company or other entity with or into which the Company may hereafter merge or consolidate or to which the Company may transfer all or substantially all of its assets, if in any such case said Company or other entity will by operation of law or expressly in writing assume all obligations of the Company hereunder as fully as if it had been originally made a party hereto, but may not otherwise assign this Agreement or its rights and obligations hereunder. Executive may not assign or transfer this Agreement or any rights or obligations hereunder, other than to Executive's estate upon Executive's death.

7.9 Choice of Law. All questions concerning the construction, validity and interpretation of this Agreement will be governed by the law of the Commonwealth of Massachusetts.

7.10 Resolution of Disputes. To ensure timely and economical resolution of any disputes that may arise in connection with Executive's employment with the Company, as a condition of Executive's employment, Executive and the Company hereby agree that any and all claims, disputes or controversies of any nature whatsoever arising out of, or relating to, this Agreement, or its interpretation, enforcement, breach, performance or execution, Executive's employment with the Company, or the termination of such employment, will be resolved, to the fullest extent permitted by law, by final, binding and confidential arbitration conducted before a single arbitrator by Judicial Arbitration and Mediation Services, Inc. ("***JAMS***") or its successor, under then applicable JAMS rules. The arbitration will take place in Boston, Massachusetts; *provided, however*, that if the arbitrator determines there will be an undue hardship to Executive to have the arbitration in such location, the arbitrator will choose an alternative appropriate location. Executive and the Company each acknowledge that by agreeing to this arbitration procedure, both Executive and the Company waive the right to resolve any such dispute, claim or demand through a trial by jury or judge or by administrative proceeding. Executive will have the right to be represented by legal counsel at Executive's expense at any arbitration proceeding. The arbitrator will: (i) have the authority to compel adequate discovery for the resolution of the dispute and to award such relief as would otherwise be available under applicable law in a court proceeding; and (ii) issue a written statement signed by the arbitrator regarding the disposition of each claim and the relief, if any, awarded as to each claim, the reasons for the award, and the arbitrator's essential findings and conclusions on which the award is based. The arbitrator, and not a court, will also be authorized to determine whether the provisions of this paragraph apply to a dispute, controversy, or claim sought to be resolved in accordance with these arbitration procedures. The Company will pay all costs and fees in excess of the amount of court fees that Executive would be required to incur if the dispute were filed or decided in a court of law. Nothing in this Agreement is intended to prevent either Executive or the Company from obtaining injunctive relief in court to prevent irreparable harm pending the conclusion of any arbitration.

IN WITNESS WHEREOF, the parties have executed this Employment Agreement effective as of the day and year first written above.

ENTASIS THERAPEUTICS HOLDINGS INC.

By: /s/ Manoussos Perros, Ph.D.
Manoussos Perros, Ph.D.
President and Chief Executive Officer

EXECUTIVE

/**s**/ Ruben Tommasi, Ph.D.
Ruben Tommasi, Ph.D.

DNDi

Drugs for Neglected Diseases *initiative*

GARDP
Global Antibiotic Research & Development Partnership

ENTASIS THERAPEUTICS LIMITED

1 Ashely Road, 3rd Floor

Altrincham, Chestshire WA14 2DT

11 January 2019

Purpose: Novation of contract

Dear Manos Perros,

We refer to the contract between ENTASIS THERAPEUTICS LIMITED **("ENTASIS")** and the Drugs for Neglected Diseases initiative **("DNDi")** for a collaboration agreement relating to the development, manufacture and commercialization of zoliflodacin, dated 4 July 2017 **("Contract").**

The GARDP Foundation, a Swiss charitable foundation having its principal office at 15 Chemin Louis-Dunant, 1202 Geneva, Switzerland (the **"GARDP Foundation")** has now been established and operationalised. In accordance with section 16.4 of the Contract, DNDi now wishes to transfer its rights, obligations and liabilities under the Contract to the GARDP Foundation under the terms set out below.

With effect from January 2019 **("Effective Date"):**

- DNDi transfers all its rights and obligations under the Contract to the GARDP Foundation.
- The GARDP Foundation will perform the Contract and be bound by its terms in every way as if it were the original party to it in place of DNDi.
- ENTASIS will perform the Contract and be bound by its terms in every way as if the GARDP Foundation were the original party to it in place of DNDi.

In addition, also with effect from the Effective Date:

- Each of ENTASIS and DNDi releases and discharges the other from all claims and demands under or in connection with the Contract, whether arising before, on, or after the Effective Date, and in each case whether known or unknown to the releasing party.
- Each of ENTASIS and the GARDP Foundation will have the right to enforce the Contract and pursue any claims and demands under it against each other with respect to matters arising before, on or after the Effective Date, as if GARDP were the original party to the Contract instead of DNDi.
- The GARDP Foundation agrees to indemnify DNDi against any losses, damages or costs suffered or incurred by DNDi under or in connection with the Contract after the Effective Date. This indemnity shall apply even if DNDi has been negligent.

The Contract will in all other respects continue on its existing terms.

From the Effective Date, each of ENTASIS and the GARDP Foundation should deal solely with each other in respect of the Contract; all invoices and correspondence relating to the Contract should be sent to the GARDP Foundation at the address set out below, marked for the attention of Jean-Pierre PACCAUD, BD Director.

If you have any questions concerning the transfer, please contact GARDP Legal Department at [***] or Fiona Ross, Senior Legal Counsel for DNDi on [***] or at [***].

This letter and any dispute or claim (including non-contractual disputes or claims) arising out of or in connection with it or its subject matter or formation shall be governed by and construed in accordance with the law of England and Wales.

Please sign each of the three (3) originals of this letter to acknowledge your agreement to the novation of the Contract with effect from the Effective Date on the terms set out above, and return two (2) originals to the attention of GARDP FOUNDATION, Legal Department, at the following address: 15 Chemin Louis Dunant, 1202 GENEVA, SWITZERLAND.

Yours faithfully

/s/ Bernard Pecoul

Name: BERNARD PECOUL

Title: EXECUTIVE DIRECTOR

for and on behalf of the **GARDP Foundation**

Signed /s/ Dr. Manica Balasegaram

Name: Dr.MANICA BALASEGARAM

Title: EXECUTIVE DIRECTOR

for and on behalf of **ENTASIS**

Signed /s/ Manos Perros

Name :MANOS PERROS

Title: CHIEF EXECUTIVE OFFICER

Exhibit 21.1

SUBSIDIARIES OF ENTASIS THERAPEUTICS HOLDINGS INC.

Name	Jurisdiction of Incorporation
Entasis Therapeutics Inc.	Delaware
Entasis Therapeutics Limited	United Kingdom
Entasis Therapeutics Security Corporation	Massachusetts

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Entasis Therapeutics Holdings Inc.:

We consent to the incorporation by reference in the registration statement No. 333-228384 on Form S-8 of Entasis Therapeutics Holdings Inc., of our report dated March 29, 2019, with respect to the consolidated balance sheets of Entasis Therapeutics Holdings Inc. and subsidiaries as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements), which report appears in the December 31, 2018 annual report on Form 10-K of Entasis Therapeutics Holdings Inc.

/s/ KPMG LLP

Cambridge, Massachusetts
March 29, 2019

Exhibit 31.1

CERTIFICATION PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Manoussos Perros, certify that:

1. I have reviewed this Annual Report on Form 10-K of Entasis Therapeutics Holdings Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 29, 2019

By: /s/ Manoussos Perros, Ph.D.
Manoussos Perros, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Michael Gutch, certify that:

1. I have reviewed this Annual Report on Form 10-K of Entasis Therapeutics Holdings Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 29, 2019

By:/s/ Michael Gutch, Ph.D.
Michael Gutch, Ph.D.
Chief Financial Officer and Chief Business Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Entasis Therapeutics Holdings Inc. (the "Company") for the year ended December 31, 2018, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his or her knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 29, 2019

By: /s/ Manoussos Perros, Ph.D.

Manoussos Perros, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 29, 2019

By: /s/ Michael Gutch, Ph.D.

Michael Gutch, Ph.D.
Chief Financial Officer and Chief Business Officer
(Principal Financial and Accounting Officer)